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NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	OCT 02	CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt
NEWS 3	OCT 19	BEILSTEIN updated with new compounds
NEWS 4	NOV 15	Derwent Indian patent publication number format enhanced
NEWS 5	NOV 19	WPIX enhanced with XML display format
NEWS 6	NOV 30	ICSD reloaded with enhancements
NEWS 7	DEC 04	LINPADOCDB now available on STN
NEWS 8	DEC 14	BEILSTEIN pricing structure to change
NEWS 9	DEC 17	USPATOLD added to additional database clusters
NEWS 10	DEC 17	IMSDRUGCONF removed from database clusters and STN
NEWS 11	DEC 17	DGENE now includes more than 10 million sequences
NEWS 12	DEC 17	TOXCENTER enhanced with 2008 MeSH vocabulary in MEDLINE segment
NEWS 13	DEC 17	MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary
NEWS 14	DEC 17	CA/CAplus enhanced with new custom IPC display formats
NEWS 15	DEC 17	STN Viewer enhanced with full-text patent content from USPATOLD
NEWS 16	JAN 02	STN pricing information for 2008 now available
NEWS 17	JAN 16	CAS patent coverage enhanced to include exemplified prophetic substances
NEWS 18	JAN 28	USPATFULL, USPAT2, and USPATOLD enhanced with new custom IPC display formats
NEWS 19	JAN 28	MARPAT searching enhanced
NEWS 20	JAN 28	USGENE now provides USPTO sequence data within 3 days of publication
NEWS 21	JAN 28	TOXCENTER enhanced with reloaded MEDLINE segment
NEWS 22	JAN 28	MEDLINE and LMEDLINE reloaded with enhancements
NEWS 23	FEB 08	STN Express, Version 8.3, now available
NEWS 24	FEB 20	PCI now available as a replacement to DPCI
NEWS 25	FEB 25	IFIREF reloaded with enhancements
NEWS 26	FEB 25	IMSPRODUCT reloaded with enhancements
NEWS 27	FEB 29	WPINDEX/WPIDS/WPIX enhanced with ECLA and current U.S. National Patent Classification
NEWS 28	MAR 31	IFICDB, IFIPAT, and IFIUDB enhanced with new custom IPC display formats
NEWS 29	MAR 31	CAS REGISTRY enhanced with additional experimental spectra
NEWS 30	MAR 31	CA/CAplus and CASREACT patent number format for U.S. applications updated
NEWS 31	MAR 31	LPCI now available as a replacement to LDPCI
NEWS 32	MAR 31	EMBASE, EMBAL, and LEMBASE reloaded with enhancements

NEWS EXPRESS FEBRUARY 08 CURRENT WINDOWS VERSION IS V8.3,
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FILE 'HOME' ENTERED AT 13:29:58 ON 03 APR 2008

=> File .Gerry2MBCE
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

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=> S (Gastrin OR (CCK receptor ligand)) (2A) (Mutant OR Mutein OR Variant) AND
pd<=20031022
   1 FILES SEARCHED...
L1          64 (GASTRIN OR (CCK RECEPTOR LIGAND)) (2A) (MUTANT OR MUTEIN OR
               VARIANT) AND PD<=20031022

=> Dup REM L1
PROCESSING COMPLETED FOR L1
L2           32 DUP REM L1 (32 DUPLICATES REMOVED)
                ANSWERS '1-13' FROM FILE MEDLINE
                ANSWERS '14-21' FROM FILE BIOSIS
                ANSWERS '22-29' FROM FILE CAPLUS
                ANSWERS '30-32' FROM FILE EMBASE

=> D TI L2 1-32

L2   ANSWER 1 OF 32     MEDLINE on STN                  DUPLICATE 1
TI   Insights into the regulation of gastric acid secretion through analysis of
     genetically engineered mice.

L2   ANSWER 2 OF 32     MEDLINE on STN                  DUPLICATE 2
TI   Effects of amidated gastrin and glycine-extended gastrin on cell
     proliferation and crypt fission in parenterally and orally fed rats.

L2   ANSWER 3 OF 32     MEDLINE on STN                  DUPLICATE 3
TI   CCK-B/gastrin receptors in human colorectal cancer.
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L2 ANSWER 4 OF 32 MEDLINE on STN DUPLICATE 4
TI Identification of CCK-B/gastrin receptor splice variants in human peripheral blood mononuclear cells.

L2 ANSWER 5 OF 32 MEDLINE on STN DUPLICATE 5
TI Lessons from genetically engineered animal models. III. Lessons learned from gastrin gene deletion in mice.

L2 ANSWER 6 OF 32 MEDLINE on STN DUPLICATE 6
TI The role of the cholecystokinin-B/gastrin receptor transmembrane domains in determining affinity for subtype-selective ligands.

L2 ANSWER 7 OF 32 MEDLINE on STN DUPLICATE 7
TI Chronic desensitization and down-regulation of the gastrin-releasing peptide receptor are mediated by a protein kinase C-dependent mechanism.

L2 ANSWER 8 OF 32 MEDLINE on STN DUPLICATE 8
TI Specificity of prohormone convertase endoproteolysis of progastrin in AtT-20 cells.

L2 ANSWER 9 OF 32 MEDLINE on STN DUPLICATE 9
TI Identification of gastrin molecular variants in gastrinoma syndrome.

L2 ANSWER 10 OF 32 MEDLINE on STN DUPLICATE 10
TI Molecular forms of gastrin in peptic ulcer: comparison of serum and tissue concentrations of G17 and G34 in gastric and duodenal ulcer subjects.

L2 ANSWER 11 OF 32 MEDLINE on STN DUPLICATE 11
TI Comparison of vagal and meat stimulation on gastric acid secretion and serum gastrin.

L2 ANSWER 12 OF 32 MEDLINE on STN DUPLICATE 12
TI Circulation gastrin variants in the cat [proceedings].

L2 ANSWER 13 OF 32 MEDLINE on STN DUPLICATE 13
TI Immunoreactive gastrin variants in cat serum.

L2 ANSWER 14 OF 32 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI Cancer-specific gastrin receptor splice variant exhibits an enhanced rate of resensitization.

L2 ANSWER 15 OF 32 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI GASTRIN EXPRESSION IS REGULATED BY THE INTERPLAY OF TGF-BETA/SMADS AND WNT PATHWAYS.

L2 ANSWER 16 OF 32 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI REGULATION OF THE GASTRIN PROMOTER BY AP1 AT SP1 DNA ELEMENTS.

L2 ANSWER 17 OF 32 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI The wild type gastrin receptor but not a colon cancer-derived gastrin receptor mutant mediates a pro-apoptotic effect of gastrin in colorectal cancer cells.

L2 ANSWER 18 OF 32 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI A novel cholecystokinin-B/gastrin receptor splice variant is expressed in human colon cancers.

L2 ANSWER 19 OF 32 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI Identification of CCK-B/gastrin receptor splice variants in human peripheral blood mononuclear cells (PBMC).

L2 ANSWER 20 OF 32 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI The functional properties of a mutant CCK-B/gastrin receptor suggest novel mechanisms underlying peptide hormone receptor activation.

L2 ANSWER 21 OF 32 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI CIRCULATING GASTRIN VARIANTS IN THE CAT.

L2 ANSWER 22 OF 32 CAPLUS COPYRIGHT 2008 ACS on STN
TI Identification of CCK-B/gastrin receptor splice variants in human peripheral blood mononuclear cells. [Erratum to document cited in CA135:352928]

L2 ANSWER 23 OF 32 CAPLUS COPYRIGHT 2008 ACS on STN
TI Enrichment method for variant proteins with altered binding properties

L2 ANSWER 24 OF 32 CAPLUS COPYRIGHT 2008 ACS on STN
TI Significance of the gastrin homology and surrounding sequences in polyomavirus middle T antigen for cell transformation

L2 ANSWER 25 OF 32 CAPLUS COPYRIGHT 2008 ACS on STN
TI Bile reflux: a possible cause of stomach ulcer in nontreated mutant mice of W/WV genotype

L2 ANSWER 26 OF 32 CAPLUS COPYRIGHT 2008 ACS on STN
TI Pituitary-induced alterations in gastrin levels and gastrointestinal growth in normal and genetically dwarf mice

L2 ANSWER 27 OF 32 CAPLUS COPYRIGHT 2008 ACS on STN
TI Gastric acid- and pepsin-stimulating activity of gastrin fragments in the cat

L2 ANSWER 28 OF 32 CAPLUS COPYRIGHT 2008 ACS on STN
TI Circulating gastrin variants in the cat

L2 ANSWER 29 OF 32 CAPLUS COPYRIGHT 2008 ACS on STN
TI Nature of big big gastrin

L2 ANSWER 30 OF 32 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
TI Erratum: Identification of CCK-B/gastrin receptor splice variants in human peripheral blood mononuclear cells (Regulatory Peptides (2001) 101 (25-33) PII: S0167011501002816).

L2 ANSWER 31 OF 32 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
TI Lessons from genetically engineered animal models. III. Lessons learned from gastrin gene deletion in mice.

L2 ANSWER 32 OF 32 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
TI Immunoreactive gastrin variants in cat serum.

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STN INTERNATIONAL SESSION SUSPENDED AT 13:33:54 ON 03 APR 2008

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                      24.57      24.78

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     FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 13:30:18 ON 03 APR 2008
L1            64 S (GASTRIN OR (CCK RECEPTOR LIGAND)) (2A) (MUTANT OR MUTEIN OR
L2            32 DUP REM L1 (32 DUPLICATES REMOVED)

=> D Ibib abs L2 1,2,6,9,10,12,13,21

L2   ANSWER 1 OF 32     MEDLINE on STN                  DUPLICATE 1
ACCESSION NUMBER:   2003049345     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 12517996
TITLE:              Insights into the regulation of gastric acid secretion
                    through analysis of genetically engineered mice.
AUTHOR:             Samuelson Linda C; Hinkle Karen L
CORPORATE SOURCE:   Department of Physiology, The University of Michigan, Ann
                    Arbor, Michigan, 48109-0622, USA.. lcsam@umich.edu
SOURCE:             Annual review of physiology, (2003) Vol. 65, pp.
                    383-400.  Electronic Publication: 2002-05-01. Ref: 72
                    Journal code: 0370600. ISSN: 0066-4278.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    (RESEARCH SUPPORT, NON-U.S. GOV'T)
                    General Review; (REVIEW)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200306
ENTRY DATE:         Entered STN: 2 Feb 2003
                    Last Updated on STN: 19 Jun 2003
                    Entered Medline: 18 Jun 2003
AB   The regulation of acid secretion in the stomach involves a complex network
     of factors that stimulate secretion in response to the ingestion of a meal
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and maintain homeostasis of gastric pH. Genetically engineered mouse models have provided a new opportunity to investigate the importance and function of specific molecules and pathways involved in the regulation of acid secretion. Mouse mutants with disruptions in the three major stimulatory pathways for acid secretion in parietal cells, gastrin, histamine, and acetylcholine, have been generated. Disruption of the gastrin pathway results in a major impairment in both basal and induced acid secretion. Histamine and acetylcholine pathway mutants also have significant alterations in acid secretion, although the impairment does not appear to be as severe as in gastrin pathway mutants , perhaps due in part to the hypergastrinemia that occurs. Mice with a disruption in the somatostatin pathway have increased gastric acid secretion, which confirms an important negative regulatory role for this factor. This review discusses these genetically engineered mouse models, as well as others, that provide insight into the complex regulation of in vivo gastric acid secretion. The regulation of growth and cellular morphology of the stomach in these mouse models is also presented. In addition, transgene promoters that are expressed in the gastric epithelium are discussed because these promoters will be important tools to alter cellular physiology in new mouse models in the future.

L2 ANSWER 2 OF 32 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2002621985 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12379816
TITLE: Effects of amidated gastrin and glycine-extended gastrin on cell proliferation and crypt fission in parenterally and orally fed rats.
AUTHOR: FitzGerald Anthony J; Ghatei Mohammad A; Mandir Nikki; Bloom Steven R; Iversen Leslie; Goodlad Robert A
CORPORATE SOURCE: Department of Histopathology, Imperial College School of Medicine, Hammersmith Hospital, London, UK.
SOURCE: Digestion, (2002) Vol. 66, No. 1, pp. 58-66.
Journal code: 0150472. ISSN: 0012-2823.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 17 Oct 2002
Last Updated on STN: 24 May 2003
Entered Medline: 23 May 2003
AB BACKGROUND/AIMS: It has been suggested that processing variants of gastrin, such as glycine-extended gastrin (G17-Gly), are enterotrophic to the colon. METHODS: Cell proliferation and crypt branching were studied in total parenteral nutrition (TPN) and orally fed rats after infusion of G17-Gly or gastrin-17. RESULTS: Gastrin produced an increase in the weight of the stomach and small intestine and a marked proliferative action on the proximal small intestine, which diminished distally. No proliferative effects of gastrin were seen in the colon. G17-Gly was associated with a small, but significant, increase in colonic weight but had little effect on cell proliferation, except in the gastric fundus. In the distal colon, G17-Gly was associated with a significant decrease in proliferation. Neither agent affected crypt branching in the small intestine or colon, but both proliferation and branching were significantly decreased by TPN. CONCLUSION: Gastrin was trophic to the stomach and the proximal small intestine but not the colon. G17-Gly had only modest proliferative actions on the intestinal epithelium in this study.

L2 ANSWER 6 OF 32 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 95197485 MEDLINE

DOCUMENT NUMBER: PubMed ID: 7890609
TITLE: The role of the cholecystokinin-B/gastrin receptor transmembrane domains in determining affinity for subtype-selective ligands.
AUTHOR: Kopin A S; McBride E W; Quinn S M; Kolakowski L F Jr; Beinborn M
CORPORATE SOURCE: Division of Gastroenterology, New England Medical Center, Tufts University School of Medicine, Boston, Massachusetts 02111.
CONTRACT NUMBER: DK01935 (United States NIDDK)
DK46767 (United States NIDDK)
P30-DK34928 (United States NIDDK)
SOURCE: The Journal of biological chemistry, (1995 Mar 10) Vol. 270, No. 10, pp. 5019-23.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199504
ENTRY DATE: Entered STN: 27 Apr 1995
Last Updated on STN: 27 Apr 1995
Entered Medline: 14 Apr 1995

AB We have examined the role of transmembrane domain amino acids in conferring subtype-selective ligand affinity to the human cholecystokinin-B (CCK-B)/gastrin receptor. Fifty-eight residues were sequentially replaced by the corresponding amino acids from the pharmacologically distinct CCK-A receptor subtype. 125I-CCK-8 competition binding experiments were performed to compare all mutant CCK-B/gastrin receptor constructs with the wild type control. Affinities for the nonselective agonist, CCK-8, as well as the subtype-selective peptide (gastrin), peptide-derived (PD135,158), and nonpeptide (L365,260) and L364,718) ligands were assessed. All of the mutants retained relatively high affinity for CCK-8, suggesting that the tertiary structure of these receptors was well maintained. Only eight of the amino acid substitutions had a significant effect on subtype selective binding. When compared with the wild type, single point mutations in the CCK-B/gastrin receptor decreased affinity for gastrin, L365,260, and PD135,158 up to 17-,23-, and 61-fold, respectively. In contrast, the affinity for L364,718 increased up to 63-fold. None of the single amino acid substitutions, however, was sufficient to fully account for the subtype selectivity of any tested compound. Rather, CCK-B/gastrin receptor affinity appears to be influenced by multiple residues acting in concert. The 8 pharmacologically important amino acids cluster in the portion of the transmembrane domains adjacent to the cell surface. The spatial orientation of these residues was analyzed with a rhodopsin-based three-dimensional model of G-protein coupled receptor structure (Baldwin, J.M. (1993) EMBO J. 12, 1693-1703). This model predicts that the 8 crucial residues project into a putative ligand pocket, similar to the one which is well established for biogenic amine receptors (Caron, M. G., and Lefkowitz, R.J. (1993) Recent Prog. Horm. Res. 48, 277-290; Strader, C.D., Sigal, I.S., and Dixon, R.A. (1989) Trends Pharmacol. Sci. 10, Dec. Suppl., 26-30).

L2 ANSWER 9 OF 32 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 87205279 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3554401
TITLE: Identification of gastrin molecular variants in gastrinoma syndrome.

AUTHOR: Kothary P C; Mahoney W C; Vinik A I
CONTRACT NUMBER: 5MO1-RR00042-22 (United States NCRR)
SOURCE: Regulatory peptides, (1987 Feb) Vol. 17, No. 2, pp. 71-84.
Journal code: 8100479. ISSN: 0167-0115.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198706
ENTRY DATE: Entered STN: 3 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 2 Jun 1987

AB The molecular species of gastrin in the circulation and in tumor extracts were studied in two groups of patients: (1) with benign gastrinoma and (2) with gastrinoma with liver metastases. Radioimmunoassays (RIAs) and immunoaffinity chromatography for the amino (NH2)- and amidated COOH-terminus of gastrin-17 (antiserum G17) and the NH2-terminus of gastrin-34 (antiserum G34) were employed. In both benign and metastatic tumors the molecular forms of gastrin in boiling water extracts measured by the gastrin-17 NH2- and COOH-terminal assays were similar. In addition to a molecular component resembling the amidated gastrin-17, there were also significant amounts of larger molecular weight (mol. weight) forms. The larger mol. weight forms absorbed by the NH2-terminus of G17 antiserum corresponded to the COOH-terminus-extended forms of gastrin-17. Furthermore, larger mol. weight gastrins immunopurified by antiserum to the NH2-terminus of gastrin-34 corresponded to gastrin-34 extended molecules. Sera of patients with liver metastases had higher concentrations of the NH2-terminal of gastrin-17 whereas sera of patients with benign gastrinoma contained predominantly gastrins detected by the COOH-terminal assay. These results suggest that: (a) there are differences in the molecular pattern of gastrin in the circulation of patients with benign and metastatic gastrinomas; (b) gastrins which are fully processed with carboxy-terminal amidation predominate in the circulation of patients with benign gastrinoma; and (c) gastrins containing the gastrin-17 and COOH-terminally extended gastrin-17 and gastrin-34 precursor molecules occur in high concentration in the circulation of gastrinoma patients with metastases to the liver.

L2 ANSWER 10 OF 32 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 81164638 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6783421
TITLE: Molecular forms of gastrin in peptic ulcer: comparison of serum and tissue concentrations of G17 and G34 in gastric and duodenal ulcer subjects.
AUTHOR: Calam J; Dockray G J; Walker R; Tracy H J; Owens D
SOURCE: European journal of clinical investigation, (1980 Jun) Vol. 10, No. 3, pp. 241-7.
Journal code: 0245331. ISSN: 0014-2972.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198106
ENTRY DATE: Entered STN: 16 Mar 1990
Last Updated on STN: 16 Mar 1990
Entered Medline: 23 Jun 1981

AB We have studied the relationships between the main molecular forms of gastrin (G17 and G34) in the serum, antral and duodenal mucosa of duodenal

(DU) and gastric (GU) ulcer patients. Fasting serum G17 was similar in both DU and GU (about 6 pmol/l) and in both groups increased about three-fold with feeding. In contrast, basal serum G34 was significantly higher in GU (29 pmol/l) than in DU (12 pmol/l) and the peak post prandial increase over basal of G34 was also higher in GU (57 pmol/l) compared with DU (10 pmol/l). In sharp contrast, in the same groups of DU and GU patients mean total antral gastrin concentrations were similar (about 12 nmol/g), and in both groups 95% of antral gastrin was G17, most of the remainder being G34. In both groups total duodenal gastrin concentrations were about 20% those in antral mucosa and about 70% of duodenal gastrin was attributable to G34. The higher serum G34 in GU could therefore be explained by increased secretion of duodenal gastrin, but further work is needed to examine whether there might also be preferential secretion of antral G34 in GU, or a difference in the metabolism (or volume of distribution) of gastrin variants in GU and DU.

L2 ANSWER 12 OF 32 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 77096518 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1011143
TITLE: Circulation gastrin variants in the cat [proceedings].
AUTHOR: Blair E L; Grund E R; Lund P K; Sanders D J
SOURCE: The Journal of physiology, (1976 Dec) Vol. 263, No. 1, pp. 194P-195P.
Journal code: 0266262. ISSN: 0022-3751.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197703
ENTRY DATE: Entered STN: 13 Mar 1990
Last Updated on STN: 13 Mar 1990
Entered Medline: 31 Mar 1977

L2 ANSWER 13 OF 32 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 75171986 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1138061
TITLE: Immunoreactive gastrin variants in cat serum.
AUTHOR: Blair E L; Grund E R; Lund P K; Reed J D; Sanders D J
SOURCE: The Journal of physiology, (1975 May) Vol. 247, No. 1, pp. 33P-34P.
Journal code: 0266262. ISSN: 0022-3751.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197509
ENTRY DATE: Entered STN: 10 Mar 1990
Last Updated on STN: 10 Mar 1990
Entered Medline: 9 Sep 1975

L2 ANSWER 21 OF 32 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 1978:3908 BIOSIS
DOCUMENT NUMBER: PREV197814003908; BR14:3908
TITLE: CIRCULATING GASTRIN VARIANTS IN THE CAT.
AUTHOR(S): BLAIR E L; GRUND E R; LUND P K; SANDERS D J
SOURCE: Gastroenterology, (1977) Vol. 73, No. 4 PART 2, pp. A-2-812.

CODEN: GASTAB. ISSN: 0016-5085.
DOCUMENT TYPE: Article
FILE SEGMENT: BR
LANGUAGE: Unavailable

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SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 13:38:56 ON 03 APR 2008

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AT 14:34:14 ON 03 APR 2008
FILE 'MEDLINE' ENTERED AT 14:34:14 ON 03 APR 2008
FILE 'BIOSIS' ENTERED AT 14:34:14 ON 03 APR 2008
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FULL ESTIMATED COST	29.23	29.44

=> D Hist

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FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 13:30:18 ON 03 APR 2008
L1 64 S (GASTRIN OR (CCK RECEPTOR LIGAND)) (2A) (MUTANT OR MUTEIN OR
L2 32 DUP REM L1 (32 DUPLICATES REMOVED)

=> S (Islet neogenesis) (5A) (Gastrin OR CCK)
L3 18 (ISLET NEOGENESIS) (5A) (GASTRIN OR CCK)

=> Dup Rem l3
PROCESSING COMPLETED FOR L3
L4 10 DUP REM L3 (8 DUPLICATES REMOVED)
ANSWERS '1-3' FROM FILE MEDLINE
ANSWERS '4-5' FROM FILE BIOSIS
ANSWERS '6-10' FROM FILE CAPLUS

=> D Ibib Abs L4 1-10

L4 ANSWER 1 OF 10 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2006022191 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16409149
TITLE: Therapeutic approaches to preserve islet mass in type 2 diabetes.
AUTHOR: Baggio Laurie L; Drucker Daniel J
CORPORATE SOURCE: Department of Medicine, Toronto General Hospital, Banting

and Best Diabetes Center, University of Toronto, Toronto, Ontario, Canada M5S 2S2.
SOURCE: Annual review of medicine, (2006) Vol. 57, pp. 265-81.
Ref: 132
Journal code: 2985151R. ISSN: 0066-4219.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200605
ENTRY DATE: Entered STN: 14 Jan 2006
Last Updated on STN: 5 May 2006
Entered Medline: 4 May 2006

AB Type 2 diabetes is characterized by hyperglycemia resulting from insulin resistance in the setting of inadequate beta-cell compensation. Currently available therapeutic agents lower blood glucose through multiple mechanisms but do not directly reverse the decline in beta-cell mass. Glucagon-like peptide-1 (GLP-1) receptor agonists, exemplified by Exenatide (exendin-4), not only acutely lower blood glucose but also engage signaling pathways in the islet beta-cell that lead to stimulation of beta-cell replication and inhibition of beta-cell apoptosis. Similarly, glucose-dependent insulinotropic polypeptide (GIP) receptor activation stimulates insulin secretion, enhances beta-cell proliferation, and reduces apoptosis. Moreover, potentiation of the endogenous postprandial levels of GLP-1 and GIP via inhibition of dipeptidyl peptidase-IV (DPP-IV) also expands beta-cell mass via related mechanisms. The thiazolidinediones (TZDs) enhance insulin sensitivity, reduce blood glucose levels, and also preserve beta-cell mass, although it remains unclear whether TZDs affect beta-cell mass via direct mechanisms. Complementary approaches to regeneration of beta-cell mass involve combinations of factors, exemplified by epidermal growth factor and gastrin, which promote islet neogenesis and ameliorate diabetes in rodent studies. Considerable preclinical data support the concept that one or more of these therapeutic approaches, alone or in combination, may potentially reverse the decline in beta-cell mass that is characteristic of the natural history of type 2 diabetes.

L4 ANSWER 2 OF 10 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2003455547 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14517799
TITLE: Hypoglycemia, defective islet glucagon secretion, but normal islet mass in mice with a disruption of the gastrin gene.
AUTHOR: Boushey Robin P; Abadir Amir; Flamez Daisy; Baggio Laurie L; Li Yazhou; Berger Veerle; Marshall Bess A; Finegood Diane; Wang Timothy C; Schuit Frans; Drucker Daniel J
CORPORATE SOURCE: Department of Medicine, Banting and Best Diabetes Centre, Toronto General Hospital, University of Toronto, Toronto, Ontario, Canada.
CONTRACT NUMBER: 1K09DK/HD02339-01 (United States NIDDK)
SOURCE: Gastroenterology, (2003 Oct) Vol. 125, No. 4, pp. 1164-74.
Journal code: 0374630. ISSN: 0016-5085.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200310
ENTRY DATE: Entered STN: 1 Oct 2003
Last Updated on STN: 31 Oct 2003

Entered Medline: 30 Oct 2003

AB BACKGROUND AND AIMS: Both cholecystokinin (CCK)-A and CCK-B receptors are expressed in the pancreas, and exogenous gastrin administration stimulates glucagon secretion from human islets. Although gastrin action has been linked to islet neogenesis, transdifferentiation, and beta-cell regeneration, an essential physiologic role(s) for gastrin in the pancreas has not been established. METHODS: We examined glucose homeostasis, glucagon gene expression, glucagon secretion, and islet mass in mice with a targeted gastrin gene disruption. RESULTS: Gastrin -/- mice exhibit fasting hypoglycemia and significantly reduced glycemic excursion following glucose challenge. Insulin sensitivity was normal and levels of circulating insulin and insulin messenger RNA transcripts were appropriately reduced in gastrin -/- mice. In contrast, levels of circulating glucagon and pancreatic glucagon messenger RNA transcripts were not up-regulated in hypoglycemic gastrin -/- mice. Furthermore, the glucagon response to epinephrine in isolated perifused islets was moderately impaired in gastrin -/- versus gastrin +/+ islets (40% reduction; $P < 0.01$, gastrin +/+ vs. gastrin -/- mice). Moreover, the glucagon response but not the epinephrine response to hypoglycemia was significantly attenuated in gastrin -/- compared with gastrin +/+ mice ($P < 0.05$). Despite gastrin expression in the developing fetal pancreas, beta-cell area, islet topography, and the islet proliferative response to experimental injury were normal in gastrin -/- mice. CONCLUSIONS: These findings show an essential physiologic role for gastrin in glucose homeostasis; however, the gastrin gene is not essential for murine islet development or the adaptive islet proliferative response to beta-cell injury.

L4 ANSWER 3 OF 10 MEDLINE on STN DUPLICATE 3

ACCESSION NUMBER: 2003169850 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12688387
TITLE: Pharmacological treatment of chronic diabetes by stimulating pancreatic beta-cell regeneration with systemic co-administration of EGF and gastrin.
AUTHOR: Brand Stephen J; Tagerud Sven; Lambert Philip; Magil Sheila G; Tatarkiewicz Krystyna; Doiron Kathryn; Yan Yanhua
CORPORATE SOURCE: Waratah Pharmaceuticals Corp, Woburn, MA 01801, USA.. sbrand@attglobal.net
SOURCE: Pharmacology & toxicology, (2002 Dec) Vol. 91, No. 6, pp. 414-20. Ref: 19
Journal code: 8702180. ISSN: 0901-9928.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200304
ENTRY DATE: Entered STN: 16 Apr 2003
Last Updated on STN: 23 Apr 2003
Entered Medline: 22 Apr 2003

AB Transgenic expression of gastrin and EGF receptor ligands stimulates islet neogenesis in adult mice, significantly increasing islet mass. The present study aimed to determine whether pharmacological treatment with gastrin and EGF can significantly stimulate beta-cell regeneration in chronic, severe insulin-dependent diabetes. Diabetes was induced by intravenous streptozotocin, resulting in >95% beta cell destruction. Four weeks later, blood glucose levels were restored to normal range by exogenous insulin therapy and rats were treated with EGF/gastrin in combination, gastrin alone, or EGF alone given subcutaneously. After 14 days treatment blood glucose was significantly lower in the EGF/gastrin group compared to the untreated diabetic controls. Along with improved glucose tolerance, EGF/gastrin treatment

significantly increased plasma C peptide and pancreatic insulin content compared to diabetic controls. Histological analysis showed that EGF/gastrin treatment significantly increased beta-cell mass as determined by point counting morphometrics. The EGF/gastrin group had a significantly greater number of BrdU labelled beta-cells/section consistent with stimulation of beta-cell replication or neogenesis. An increased number of gastrin receptor positive cells were observed in the EGF/gastrin-treated groups. In contrast to the effectiveness of the EGF/gastrin combination, neither gastrin nor EGF alone improved glucose tolerance in severely streptozotocin-diabetic rats. These studies indicate that physiologically significant improvement in glucose tolerance can be achieved through stimulating beta-cell regeneration with gastrin/EGF administered systemically as conventional pharmacological therapy.

L4 ANSWER 4 OF 10 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:326613 BIOSIS
DOCUMENT NUMBER: PREV200600331987
TITLE: Prolonged efficacy of islet neogenesis therapy methods with a gastrin/CCK receptor ligand and an EGF receptor ligand composition in subjects with preexisting diabetes.
AUTHOR(S): Brand, Stephen J. [Inventor]
CORPORATE SOURCE: Lincoln, MA USA
ASSIGNEE: Waratah Pharmaceuticals, Inc.
PATENT INFORMATION: US 06992060 20060131
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (JAN 31 2006)
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 28 Jun 2006
Last Updated on STN: 28 Jun 2006
AB Compositions and methods are provided for achieving in vivo islet cell regeneration in subjects with preexisting diabetes. The methods comprise short term treatment with a composition having a gastrin/cholecystokinin receptor ligand and an EGF receptor ligand. Treatment with such a composition for a short term resulted in a prolonged period of increased insulin release, decreased fasting blood glucose, and improved glucose tolerance, the prolonged efficacy, the period being considered from the time of cessation of treatment.

L4 ANSWER 5 OF 10 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:441681 BIOSIS
DOCUMENT NUMBER: PREV200100441681
TITLE: Prolonged efficacy of islet neogenesis therapy with gastrin and TGFalpha in mature rats with preexisting diabetes.
AUTHOR(S): Brand, Stephen J. [Reprint author]; Talbot, Diane [Reprint author]; Doiron, Kathryn [Reprint author]
CORPORATE SOURCE: Lexington, MA, USA
SOURCE: Diabetes, (June, 2001) Vol. 50, No. Supplement 2, pp. A338. print.
Meeting Info.: 61st Scientific Sessions of the American Diabetes Association. Philadelphia, Pennsylvania, USA. June 22-26, 2001. American Diabetes Association.
CODEN: DIAEAZ. ISSN: 0012-1797.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 19 Sep 2001

Last Updated on STN: 22 Feb 2002

L4 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1001979 CAPLUS
DOCUMENT NUMBER: 147:439323
TITLE: Too many notes: up and down the scales of diabetes therapy
AUTHOR(S): Vinik, Aaron
CORPORATE SOURCE: Strelitz Diabetes Research Institute, Eastern Virginia Medical School, Norfolk, VA, USA
SOURCE: Clinical Therapeutics (2007), 29(Theme Iss.), 1227-1235
CODEN: CLTHDG; ISSN: 0149-2918
PUBLISHER: Excerpta Medica, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Some concerns on the prevention and treatment of diabetes are examined The greatest problem in preventing diabetes is recognizing which patients are at risk for the development of this disease. The Diabetes Prevention Program (DPP) has indicated that with therapeutic lifestyle changes, the conversion of impaired glucose tolerance (IGT) to diabetes could be reduced by 58%. Although the message from the DPP is quite clear and similar redns. of 58% in the development of diabetes were found in other recent studies, it is easier for people to pop a pill than to embark on an intensive change in their lifestyle. The findings of the Heart Outcomes Prevention Evaluation (HOPE) and the Microalbuminuria, Cardiovascular, and Renal Outcomes in HOPE studies suggested that the use of an angiotensin-converting enzyme (ACE) inhibitor (ramipril) was associated with a reduction in conversion of IGT to diabetes. This prospect also became evident in the Diabetes Risk Evaluation and Microalbuminuria (DREAM) study, a 2-factor trial comparing rosiglitazone and ramipril vs. placebo. The recognition of the fact that, no matter the degree of insulin resistance, people do not develop diabetes unless there is failure of the β-cell, it must remain an axiom that treating diabetes will require fixing the β-cell.
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:227274 CAPLUS
DOCUMENT NUMBER: 144:347805
TITLE: Islet neogenesis: A potential therapeutic tool in type 1 diabetes
AUTHOR(S): Lipsett, Mark; Aikin, Reid; Castellarin, Mauro; Hanley, Stephen; Jamal, Al-Maleek; Laganiere, Simon; Rosenberg, Lawrence
CORPORATE SOURCE: Centre for Pancreatic Diseases, McGill University Health Centre, Department of Surgery, C9-128 Montreal General Hospital, McGill University, Montreal, QC, H3G 1A4, Can.
SOURCE: International Journal of Biochemistry & Cell Biology (2006), 38(5-6), 715-720
CODEN: IJBBFU; ISSN: 1357-2725
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Current therapies for type 1 diabetes, including fastidious blood glucose monitoring and multiple daily insulin injections, are not sufficient to prevent complications of the disease. Though pancreas and possibly islet transplantation can prevent the progression of complications, the scarcity of donor organs limits widespread application of these approaches. Understanding the mechanisms of β-cell mass

expansion as well as the means to exploit these pathways has enabled researchers to develop new strategies to expand and maintain islet cell mass. Potential new therapeutic avenues include ex vivo islet expansion and improved viability of islets prior to implantation, as well as the endogenous expansion of β-cell mass within the diabetic patient. Islet neogenesis, through stem cell activation and/or transdifferentiation of mature fully differentiated cells, has been proposed as a means of β-cell mass expansion. Finally, any successful new therapy for type 1 diabetes via β-cell mass expansion will require prevention of β-cell death and maintenance of long-term endocrine function.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:368884 CAPLUS
DOCUMENT NUMBER: 140:386447
TITLE: Methods and composition for the treatment of diabetes with FACGINT (FActor for Complementing Gastrin for Islet Neogenesis Therapy)
INVENTOR(S): Brand, Stephen J.; Cruz, Antonio; Pastrak, Aleksandra; Hew, Yin
PATENT ASSIGNEE(S): Waratah Pharmaceuticals, Inc., Can.
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004037195	A2	20040506	WO 2003-US33595		20031022
WO 2004037195	A3	20050616			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2501677	A1	20040506	CA 2003-2501677		20031022
AU 2003283004	A1	20040513	AU 2003-283004		20031022
BR 2003015523	A	20050830	BR 2003-15523		20031022
EP 1569680	A2	20050907	EP 2003-774936		20031022
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
CN 1729016	A	20060201	CN 2003-80107284		20031022
JP 2006506386	T	20060223	JP 2004-547077		20031022
EP 1884247	A2	20080206	EP 2007-19263		20031121
EP 1884247	A3	20080213			
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PT, RO, SE, SI, SK, TR					
MX 2005PA04202	A	20050920	MX 2005-PA4202		20050420
IN 2005KN00910	A	20060623	IN 2005-KN910		20050517
NO 2005002419	A	20050707	NO 2005-2419		20050519
US 20060189520	A1	20060824	US 2006-532295		20060217
PRIORITY APPLN. INFO.:			US 2002-420187P	P	20021022
			US 2002-420399P	P	20021022
			US 2002-428100P	P	20021121

	US 2002-428562P	P	20021122
	US 2002-430590P	P	20021203
	WO 2003-US33595	W	20031022
	US 2003-519933P	P	20031114
	EP 2003-778179	A3	20031121

AB Compns. and methods are provided for islet neogenesis therapy comprising a member of a group of factors that complement a gastrin/CCK receptor ligand, with formulations, devices and methods for sustained release delivery and for local delivery to target organs. Methods and composition for the transplantation of stem cells and stimulation to proliferate and differentiated into insulin-producing cells are also claimed.

L4 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:991368 CAPLUS
DOCUMENT NUMBER: 140:35953
TITLE: Compositions and methods for treating diabetes via pancreatic islet neogenesis
INVENTOR(S): Brand, Stephen J.; Cruz, Antonio
PATENT ASSIGNEE(S): Waratah Pharmaceuticals, Inc., Can.
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003103701	A1	20031218	WO 2003-US18377	20030609
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2486584	A1	20031218	CA 2003-2486584	20030609
AU 2003243501	A1	20031222	AU 2003-243501	20030609
US 20040023885	A1	20040205	US 2003-457126	20030609
EP 1511509	A1	20050309	EP 2003-757483	20030609
EP 1511509	B1	20071010		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1671407	A	20050921	CN 2003-818526	20030609
JP 2005533775	T	20051110	JP 2004-510820	20030609
EP 1837031	A1	20070926	EP 2007-10865	20030609
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PT, RO, SE, SI, SK, TR				
AT 375166	T	20071015	AT 2003-757483	20030609
EP 1884247	A2	20080206	EP 2007-19263	20031121
EP 1884247	A3	20080213		
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PT, RO, SE, SI, SK, TR				
ZA 2004009490	A	20060426	ZA 2004-9490	20041124
US 20060183674	A1	20060817	US 2006-517135	20060217

PRIORITY APPLN. INFO.:	US 2002-387032P	P	20020607
	US 2002-430590P	P	20021203
	US 2002-387032	A	20020607
	US 2002-428100P	P	20021121

	US 2002-428562P	P	20021122
	US 2002-430590	A	20021203
	EP 2003-757483	A3	20030609
	WO 2003-US18377	W	20030609
	US 2003-519933P	P	20031114
	EP 2003-778179	A3	20031121

AB Compns. and methods for islet neogenesis therapy comprising an EGF and a gastrin in combination with immune suppression, and for treating or preventing early stage diabetes with a gastrin/CCK receptor ligand and an immunosuppressant are provided.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:539568 CAPLUS

DOCUMENT NUMBER: 137:103902

TITLE: Prolonged efficacy of islet neogenesis therapy methods with a gastrin/CCK receptor ligand and an EGF receptor ligand composition in subjects with preexisting diabetes

INVENTOR(S): Brand, Stephen J.

PATENT ASSIGNEE(S): Waratah Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002055152	A2	20020718	WO 2002-US685	20020111
WO 2002055152	A9	20030123		
WO 2002055152	A3	20030410		
W: AU, CA, CN, HU, IL, IN, JP, KR, NO, PH, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
CA 2434330	A1	20020718	CA 2002-2434330	20020111
AU 2002243501	A1	20020724	AU 2002-243501	20020111
AU 2002243501	B2	20071122		
US 20020098178	A1	20020725	US 2002-44048	20020111
US 6992060	B2	20060131		
EP 1351742	A2	20031015	EP 2002-708990	20020111
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
JP 2004520345	T	20040708	JP 2002-555881	20020111
IN 2003KN00875	A	20050311	IN 2003-KN875	20030708
ZA 2003005347	A	20041011	ZA 2003-5347	20030710
US 20060234932	A1	20061019	US 2005-273615	20051114

PRIORITY APPLN. INFO.:	US 2001-261638P	P	20010112
	US 2002-44048	A1	20020111
	WO 2002-US685	W	20020111

AB Compns. and methods are provided for achieving in vivo islet cell regeneration in subjects with preexisting diabetes. The methods comprise short term treatment with a composition having a gastrin/cholecystokinin receptor ligand and an EGF receptor ligand. Treatment with such a composition for a short term resulted in a prolonged period of increased insulin release, decreased fasting blood glucose, and improved glucose tolerance, the prolonged efficacy, the period being considered from the time of cessation of treatment.

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FILE 'BIOSIS' ENTERED AT 15:25:10 ON 03 APR 2008
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -4.00      -4.00

=> S (leu15-Gastrin) OR (leu-15 Gastrin)
L5          92 (LEU15-GASTRIN) OR (LEU-15 GASTRIN)

=> S L5 AND pd<=20031022
   2 FILES SEARCHED...
L6          91 L5 AND PD<=20031022

=> Dup Rem L6
PROCESSING COMPLETED FOR L6
L7           34 DUP REM L6 (57 DUPLICATES REMOVED)
                ANSWERS '1-23' FROM FILE MEDLINE
                ANSWERS '24-25' FROM FILE BIOSIS
                ANSWERS '26-29' FROM FILE CAPLUS
                ANSWERS '30-34' FROM FILE EMBASE

=> D TI L7 1-34

L7   ANSWER 1 OF 34     MEDLINE on STN                  DUPLICATE 2
TI   ECL cells of the rat stomach: development of lipofuscin in response to
     sustained gastrin stimulation.

L7   ANSWER 2 OF 34     MEDLINE on STN                  DUPLICATE 3
TI   Cholecystokinin(CCK)-A and CCK-B/gastrin receptors in human tumors.

L7   ANSWER 3 OF 34     MEDLINE on STN                  DUPLICATE 4
TI   Localization of cholecystokinin A and cholecystokinin B-gastrin receptors
     in the human stomach.
```

L7 ANSWER 4 OF 34 MEDLINE on STN DUPLICATE 5
TI Gastrin does not stimulate growth of the rat pancreas.

L7 ANSWER 5 OF 34 MEDLINE on STN DUPLICATE 6
TI Perturbations in blood Ca(2)+ do not affect the activity of rat stomach enterochromaffin-like cells.

L7 ANSWER 6 OF 34 MEDLINE on STN DUPLICATE 7
TI Time course of hypertrophic and ultrastructural responses of rat stomach enterochromaffin-like cells to sustained hypergastrinemia.

L7 ANSWER 7 OF 34 MEDLINE on STN DUPLICATE 8
TI Rat stomach enterochromaffin-like cells are not stimulated by pylorus ligation. A biochemical and ultrastructural study.

L7 ANSWER 8 OF 34 MEDLINE on STN DUPLICATE 9
TI Synthesis and characterization of a new labeled gastrin ligand, 125-I-BH-[Leu15]-gastrin-(5-17), on binding to canine fundic mucosal cells and Jurkat cells.

L7 ANSWER 9 OF 34 MEDLINE on STN DUPLICATE 10
TI Gastrin13 and the C-terminal octapeptide of cholecystokinin are differently coupled to G-proteins in guinea-pig brain membranes.

L7 ANSWER 10 OF 34 MEDLINE on STN DUPLICATE 11
TI Acute responses of rat stomach enterochromaffinlike cells to gastrin: secretory activation and adaptation.

L7 ANSWER 11 OF 34 MEDLINE on STN DUPLICATE 12
TI Use of zwitterionic detergents for the separation of closely related peptides by capillary electrophoresis.

L7 ANSWER 12 OF 34 MEDLINE on STN DUPLICATE 13
TI Distinct receptors for cholecystokinin and gastrin on canine fundic D-cells.

L7 ANSWER 13 OF 34 MEDLINE on STN DUPLICATE 14
TI Direct modulation of secretin binding sites by gastrin in the rat stomach.

L7 ANSWER 14 OF 34 MEDLINE on STN DUPLICATE 15
TI Application of 2-chlorotrityl resin in solid phase synthesis of (Leu15)-gastrin I and unsulfated cholecystokinin octapeptide. Selective O-deprotection of tyrosine.

L7 ANSWER 15 OF 34 MEDLINE on STN DUPLICATE 16
TI Evidence that gastrin enhances 45Ca uptake into bone through release of a gastric hormone.

L7 ANSWER 16 OF 34 MEDLINE on STN DUPLICATE 17
TI Trophic effects of continuous infusion of [Leu15]-gastrin-17 in the rat.

L7 ANSWER 17 OF 34 MEDLINE on STN DUPLICATE 19
TI Molecular identification and characterization of the gastrin receptor in guinea pig gastric glands.

L7 ANSWER 18 OF 34 MEDLINE on STN DUPLICATE 20
TI Effects of long-term hypergastrinaemia on the ultrastructure of enterochromaffin-like cells in the stomach of the rat, hamster and guinea pig.

L7 ANSWER 19 OF 34 MEDLINE on STN DUPLICATE 21

TI Novel activity of angiotensin-converting enzyme. Hydrolysis of cholecystokinin and gastrin analogues with release of the amidated C-terminal dipeptide.

L7 ANSWER 20 OF 34 MEDLINE on STN DUPLICATE 22
TI Biological activity of progastrin posttranslational processing intermediates.

L7 ANSWER 21 OF 34 MEDLINE on STN DUPLICATE 23
TI Gastrin receptor characterization: affinity cross-linking of the gastrin receptor on canine gastric parietal cells.

L7 ANSWER 22 OF 34 MEDLINE on STN DUPLICATE 24
TI Gastrin receptors in normal and malignant gastrointestinal mucosa: age-associated changes.

L7 ANSWER 23 OF 34 MEDLINE on STN DUPLICATE 25
TI Gastrin receptors on nonparietal cells isolated from canine fundic mucosa.

L7 ANSWER 24 OF 34 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI Gastrin-13 and the C-terminal octapeptide of cholecystokinin are differently coupled to G-proteins in guinea-pig brain membranes.

L7 ANSWER 25 OF 34 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI TROPHIC EFFECTS OF CONTINUOUS INFUSION OF LEU-15 GASTRIN-17 IN THE RAT.

L7 ANSWER 26 OF 34 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 1
TI Establishment of radioligand binding assay of gastrin receptors in rat gastric parietal cells

L7 ANSWER 27 OF 34 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 18
TI Esterification of partially protected peptide fragments with resins. Synthesis of Leu15-gastrin I using 2-chlorotrityl chloride resin

L7 ANSWER 28 OF 34 CAPLUS COPYRIGHT 2008 ACS on STN
TI Gastrin13 binds to CCKB brain membrane receptors coupled to G protein in guinea pig brain membranes

L7 ANSWER 29 OF 34 CAPLUS COPYRIGHT 2008 ACS on STN
TI A simple animal preparation to study the effect of gastrointestinal hormones and related peptides on pyloric function

L7 ANSWER 30 OF 34 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
TI Distinct receptors for cholecystokinin and gastrin on canine fundic D-cells.

L7 ANSWER 31 OF 34 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
TI Biological activity of progastrin posttranslational processing intermediates.

L7 ANSWER 32 OF 34 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
TI Gastrin receptor characterization: Affinity cross-linking of the gastrin receptor on canine gastric parietal cells.

L7 ANSWER 33 OF 34 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights

reserved on STN
TI Gastrin receptors in normal and malignant gastrointestinal mucosa: Age-associated changes.

L7 ANSWER 34 OF 34 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
TI Gastrin receptors on nonparietal cells isolated from canine fundic mucosa.

=> Log Off h
SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 15:28:06 ON 03 APR 2008

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTAEGS1646

PASSWORD:
* * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE'
AT 15:31:52 ON 03 APR 2008
FILE 'MEDLINE' ENTERED AT 15:31:52 ON 03 APR 2008
FILE 'BIOSIS' ENTERED AT 15:31:52 ON 03 APR 2008
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FILE 'CAPLUS' ENTERED AT 15:31:52 ON 03 APR 2008
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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	78.68	78.89

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-4.00	-4.00

=> D hist

(FILE 'HOME' ENTERED AT 13:29:58 ON 03 APR 2008)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 13:30:18 ON 03 APR 2008
L1 64 S (GASTRIN OR (CCK RECEPTOR LIGAND)) (2A) (MUTANT OR MUTEIN OR
L2 32 DUP REM L1 (32 DUPLICATES REMOVED)
L3 18 S (ISLET NEOGENESIS) (5A) (GASTRIN OR CCK)
L4 10 DUP REM L3 (8 DUPLICATES REMOVED)
L5 92 S (LEU15-GASTRIN) OR (LEU-15 GASTRIN)
L6 91 S L5 AND PD<=20031022
L7 34 DUP REM L6 (57 DUPLICATES REMOVED)

=> D Ibib ABS L7 4,10,43,16,31
34 ANSWERS ARE AVAILABLE. SPECIFIED ANSWER NUMBER EXCEEDS ANSWER SET SIZE
The answer numbers requested are not in the answer set.
ENTER ANSWER NUMBER OR RANGE (1):4,10,13,16,31

L7 ANSWER 4 OF 34 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 96293634 MEDLINE

DOCUMENT NUMBER: PubMed ID: 8726311
TITLE: Gastrin does not stimulate growth of the rat pancreas.
AUTHOR: Chen D; Nylander A G; Norlen P; Hakanson R
CORPORATE SOURCE: Dept. of Pharmacology, University of Lund, Sweden.
SOURCE: Scandinavian journal of gastroenterology, (1996 Apr) Vol. 31, No. 4, pp. 404-10.
Journal code: 0060105. ISSN: 0036-5521.
PUB. COUNTRY: Norway
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199609
ENTRY DATE: Entered STN: 8 Oct 1996
Last Updated on STN: 8 Oct 1996
Entered Medline: 23 Sep 1996

AB BACKGROUND: Gastrin is thought to stimulate growth of the pancreas via gastrin/cholecystokinin (CCK)-B-type receptors. The aim of the present study was to examine the trophic response of the pancreas to exogenous gastrin or to hypergastrinemia of endogenous origin and to hypogastrinemia with or without concomitant hyperCCKemia. METHODS: Hypergastrinemia was induced in male Sprague-Dawley rats by continuous infusion of human Leu15-gastrin-17 (5 nmol/kg/h, subcutaneously), by removal of the acid-producing part of the stomach (fundectomy), or by treatment with omeprazole (400 mumol/ kg/day, orally). Hypogastrinemia was induced by antrectomy or by gastrectomy. HyperCCKemia was induced by pancreaticobiliary diversion (PBD). The rats were killed 10 days or 8 weeks after the operations or treatments. The concentrations of circulating gastrin and CCK were measured by radioimmunoassay. The pancreatic weight and DNA content were determined. RESULTS: Gastrin infusion, omeprazole treatment, and fundectomy greatly increased the serum gastrin concentration. The resulting levels were very similar in the three groups and probably represent the maximum attainable physiologic serum gastrin concentration. Whereas gastrin infusion or omeprazole treatment (hypergastrinemia) and antrectomy (hypogastrinemia) were without effect on the weight and DNA content of the pancreas, gastrectomy (hypogastrinemia) and fundectomy (hypergastrinemia) increased the weight and DNA content. PBD (hyperCCKemia) greatly increased the weight and DNA content of the pancreas. PBD plus fundectomy, PBD plus gastrectomy, PBD plus antrectomy, and PBD plus omeprazole increased the weight and DNA content of the pancreas, as did PBD alone. CONCLUSION: CCK is a physiologically important trophic stimulus for the rat pancreas, but gastrin is not. The increase in pancreatic weight and DNA content after fundectomy and gastrectomy cannot be explained by means of either gastrin or CCK.

L7 ANSWER 10 OF 34 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 94291850 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7517373
TITLE: Acute responses of rat stomach enterochromaffinlike cells to gastrin: secretory activation and adaptation.
AUTHOR: Chen D; Monstein H J; Nylander A G; Zhao C M; Sundler F; Hakanson R
CORPORATE SOURCE: Department of Pharmacology, University of Lund, Sweden.
SOURCE: Gastroenterology, (1994 Jul) Vol. 107, No. 1, pp. 18-27.
Journal code: 0374630. ISSN: 0016-5085.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 199408
ENTRY DATE: Entered STN: 15 Aug 1994
Last Updated on STN: 29 Jan 1996
Entered Medline: 4 Aug 1994

AB BACKGROUND/AIMS: Evidence for gastrin-induced histamine secretion from isolated rat enterochromaffinlike (ECL) cells was presented recently. We have investigated the gastrin-evoked secretory activation and adaptation of ECL cells in intact rats over a time span of a few minutes to several hours. METHODS: Fasted rats received a maximally effective dose of synthetic human Leu15-gastrin-17 by continuous intravenous infusion. ECL cell ultrastructure and ECL cell-related parameters (e.g., mucosal histamine and pancreastatin concentrations, histidine decarboxylase [HDC] activity, and messenger RNA [mRNA] concentration) were analyzed. RESULTS: Gastrin reduced the number of cytoplasmic vesicles in ECL cells while reducing the concentrations of histamine and pancreastatin in the oxyntic mucosa. The effects were maximal within a few hours after the start of gastrin infusion. The concentration of pancreastatin in serum was elevated for the duration of the study. The mucosal concentrations of histamine and pancreastatin returned to prestimulation values after 4-6 hours. The HDC activity and mRNA concentration increased progressively until after 6-8 hours of gastrin infusion. CONCLUSIONS: Gastrin promptly degranulates the ECL cells, releasing histamine and pancreastatin from the vesicles. Synthesis of histamine and pancreastatin is accelerated, a process associated with renewal of vesicles. The increase in HDC activity and mRNA concentration continues for several hours after restoration of the vesicles.

L7 ANSWER 13 OF 34 MEDLINE on STN DUPLICATE 14
ACCESSION NUMBER: 93124366 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1479544
TITLE: Direct modulation of secretin binding sites by gastrin in the rat stomach.
AUTHOR: Iwakawa S; Nomura H; Hori R; Okumura K
CORPORATE SOURCE: Department of Hospital Pharmacy, School of Medicine, Kobe University, Japan.
SOURCE: Journal of pharmacobio-dynamics, (1992 Aug) Vol. 15, No. 8, pp. 437-41.
Journal code: 7901854. ISSN: 0386-846X.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199302
ENTRY DATE: Entered STN: 26 Feb 1993
Last Updated on STN: 26 Feb 1993
Entered Medline: 9 Feb 1993

AB The effect of gastrin on secretin binding sites in the stomach was studied using the plasma membranes from rat gastric mucosa and vascularly perfused rat stomach. Tetragastrin transiently increased secretin binding to the mucosal plasma membranes. In the perfused stomach secretin binding was also modulated by the inclusion of tetragastrin or human [Leu15] gastrin I in the perfusate. However, histamine did not show such a modulatory effect. Tetragastrin had an insignificant effect on secretin binding sites in rat pancreas. These results suggest that the direct modulation of secretin binding by gastrin to its receptors may be involved in the inhibitory action of secretin on acid secretion induced by gastrin.

L7 ANSWER 16 OF 34 MEDLINE on STN DUPLICATE 17
ACCESSION NUMBER: 90076833 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2293597
TITLE: Trophic effects of continuous infusion of [Leu15]-gastrin-17 in the rat.

AUTHOR: Ryberg B; Axelson J; Hakanson R; Sundler F; Mattsson H
CORPORATE SOURCE: Department of Biology AB Hassle, Gastrointestinal Research, Molndal, Sweden.
SOURCE: Gastroenterology, (1990 Jan) Vol. 98, No. 1, pp. 33-8.
Journal code: 0374630. ISSN: 0016-5085.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199001
ENTRY DATE: Entered STN: 28 Mar 1990
Last Updated on STN: 28 Mar 1990
Entered Medline: 16 Jan 1990

AB This report describes the trophic effects of exogenous gastrin on the digestive tract and pancreas and the effect on the density of enterochromaffinlike cells in the oxyntic mucosa of the stomach. Female rats were given 1.2 or 2.4 nmol/kg.h of synthetic human [Leu15]-gastrin-17 for 28 days (via osmotic minipumps implanted subcutaneously). As a result, measurable plasma gastrin increased from about 230 pg/ml in the controls to about 500 and 800 pg/ml in the low- and high-dose groups, respectively. The trophic effects of gastrin were reflected in increased stomach weight and oxyntic mucosal mass. Gastrin also increased the enterochromaffinlike cell density and associated parameters (histamine concentration and histidine decarboxylase activity) but was without demonstrable effects on other parts of the digestive tract and pancreas. The results show that continuous infusion of exogenous gastrin for 28 days induces trophic changes similar to those seen after a period of hypergastrinemia induced by treatment with effective inhibitors of acid secretion.

L7 ANSWER 31 OF 34 EMBASE
ACCESSION NUMBER: 1987133818 EMBASE
TITLE: Biological activity of progastrin posttranslational processing intermediates.
AUTHOR: Matsumoto, M.; Park, J.; Sugano, K.; Yamada, T.
CORPORATE SOURCE: Department of Internal Medicine, The University of Michigan Medical Center, Ann Arbor, MI 48109, United States.
SOURCE: American Journal of Physiology - Gastrointestinal and Liver Physiology, (1987) Vol. 252, No. 3, pp. 15/3.
ISSN: 0193-1857 CODEN: APGPDF
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
029 Clinical and Experimental Biochemistry
003 Endocrinology
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Dec 1991
Last Updated on STN: 11 Dec 1991

AB We recently identified carboxyl-terminally extended progastrin posttranslational processing intermediates in G cells of the gastric antrum and demonstrated that they are cosecreted with gastrin. To determine the physiological significance of these intermediates, we examined the biological activity of two synthetic gastrin precursor analogues that correspond to hexagastrin with carboxyl-terminal extensions, Tyr-Gly-Trp-Met-Asp-Phe-Gly (GL-7) and Tyr-Gly-Trp-Met-Asp-Phe-Gly-Arg-Arg (GL-9) on gastric parietal and D cells isolated from canine fundic mucosa. Both analogues were as efficacious as gastrin heptadecapeptide in displacing (125)I-[Leu(15)]

gastrin from binding sites on the two cell types and in stimulating [(14)C]aminopyrine uptake by parietal cells and somatostatin release from D cells. However, both analogues were 10(4)- to 10(5)-fold less potent than gastrin heptadecapeptide in these activities. Our results indicate that progastrin processing intermediates do not have physiologically relevant actions under normal circumstances and support the notion that carboxyl-terminally amidated peptides such as gastrin require the amide moiety for biological activity.

=> Log off h
SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 15:34:38 ON 03 APR 2008

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Welcome to STN International! Enter x:x

LOGINID:SSPTAEGS1646

PASSWORD:
* * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE'
AT 15:39:52 ON 03 APR 2008
FILE 'MEDLINE' ENTERED AT 15:39:52 ON 03 APR 2008
FILE 'BIOSIS' ENTERED AT 15:39:52 ON 03 APR 2008
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COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)
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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	87.38	87.59

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-4.00	-4.00

=> D hist

(FILE 'HOME' ENTERED AT 13:29:58 ON 03 APR 2008)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 13:30:18 ON 03 APR 2008
L1 64 S (GASTRIN OR (CCK RECEPTOR LIGAND)) (2A) (MUTANT OR MUTEIN OR
L2 32 DUP REM L1 (32 DUPLICATES REMOVED)
L3 18 S (ISLET NEOGENESIS) (5A) (GASTRIN OR CCK)
L4 10 DUP REM L3 (8 DUPLICATES REMOVED)
L5 92 S (LEU15-GASTRIN) OR (LEU-15 GASTRIN)
L6 91 S L5 AND PD<=20031022
L7 34 DUP REM L6 (57 DUPLICATES REMOVED)

=> S (Gastrin-17 OR Gastrin 17) (S) (islet neogenesis)
L8 2 (GASTRIN-17 OR GASTRIN 17) (S) (ISLET NEOGENESIS)

=> Dup rem
ENTER L# LIST OR (END):L8
PROCESSING COMPLETED FOR L8

L9 2 DUP REM L8 (0 DUPLICATES REMOVED)
ANSWERS '1-2' FROM FILE CAPLUS

=> D IBIB Abs

L9 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:368884 CAPLUS
DOCUMENT NUMBER: 140:386447
TITLE: Methods and composition for the treatment of diabetes with FACGINT (FActor for Complementing Gastrin for Islet Neogenesis Therapy)
INVENTOR(S): Brand, Stephen J.; Cruz, Antonio; Pastrak, Aleksandra; Hew, Yin
PATENT ASSIGNEE(S): Waratah Pharmaceuticals, Inc., Can.
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004037195	A2	20040506	WO 2003-US33595		20031022
WO 2004037195	A3	20050616			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2501677	A1	20040506	CA 2003-2501677		20031022
AU 2003283004	A1	20040513	AU 2003-283004		20031022
BR 2003015523	A	20050830	BR 2003-15523		20031022
EP 1569680	A2	20050907	EP 2003-774936		20031022
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
CN 1729016	A	20060201	CN 2003-80107284		20031022
JP 2006506386	T	20060223	JP 2004-547077		20031022
EP 1884247	A2	20080206	EP 2007-19263		20031121
EP 1884247	A3	20080213			
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PT, RO, SE, SI, SK, TR					
MX 2005PA04202	A	20050920	MX 2005-PA4202		20050420
IN 2005KN00910	A	20060623	IN 2005-KN910		20050517
NO 2005002419	A	20050707	NO 2005-2419		20050519
US 20060189520	A1	20060824	US 2006-532295		20060217
PRIORITY APPLN. INFO.:			US 2002-420187P	P	20021022
			US 2002-420399P	P	20021022
			US 2002-428100P	P	20021121
			US 2002-428562P	P	20021122
			US 2002-430590P	P	20021203
			WO 2003-US33595	W	20031022
			US 2003-519933P	P	20031114
			EP 2003-778179	A3	20031121

AB Compns. and methods are provided for islet neogenesis therapy comprising a member of a group of factors that complement a gastrin/CCK receptor ligand, with formulations, devices and methods for sustained release

delivery and for local delivery to target organs. Methods and composition for the transplantation of stem cells and stimulation to proliferate and differentiated into insulin-producing cells are also claimed.

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=> D Hist

     (FILE 'HOME' ENTERED AT 13:29:58 ON 03 APR 2008)

     FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 13:30:18 ON 03 APR 2008
L1           64 S (GASTRIN OR (CCK RECEPTOR LIGAND)) (2A) (MUTANT OR MUTEIN OR
L2           32 DUP REM L1 (32 DUPLICATES REMOVED)
L3           18 S (ISLET NEOGENESIS) (5A) (GASTRIN OR CCK)
L4           10 DUP REM L3 (8 DUPLICATES REMOVED)
L5           92 S (LEU15-GASTRIN) OR (LEU-15 GASTRIN)
L6           91 S L5 AND PD<=20031022
L7           34 DUP REM L6 (57 DUPLICATES REMOVED)
L8            2 S (GASTRIN-17 OR GASTRIN 17) (S) (ISLET NEOGENESIS)
L9            2 DUP REM L8 (0 DUPLICATES REMOVED)

=> S (GASTRIN-17 OR GASTRIN 17) (S) (Pancreas OR Islet)
L10         25 (GASTRIN-17 OR GASTRIN 17) (S) (PANCREAS OR ISLET)

=> Dup Rem L!)
ENTER L# LIST OR (END):L10
'L!)' IS NOT VALID.  VALID FILE NAMES ARE 'MEDLINE, BIOSIS, CAPLUS, EMBASE'
You have entered a file name of duplicates to keep that is not
referenced by any of the L#s specified for this DUPLICATE command.
The file names of duplicates that can be kept are listed above.
Please enter one of these file names.

=> Dup Rem L10
PROCESSING COMPLETED FOR L10
L11          16 DUP REM L10 (9 DUPLICATES REMOVED)
                ANSWERS '1-5' FROM FILE MEDLINE
                ANSWERS '6-15' FROM FILE CAPLUS
                ANSWER '16' FROM FILE EMBASE

=> D ibib abs L10 1-16

L10  ANSWER 1 OF 25     MEDLINE on STN
ACCESSION NUMBER:   1999343088     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 10416699
TITLE:              Expression of cholecystokinin in the pancreas during
                    development.
AUTHOR:             Shimizu K; Shiratori K; Sakayori N; Kobayashi M; Hayashi N
CORPORATE SOURCE:   Department of Gastroenterology, Tokyo Women's Medical
                    University, School of Medicine, Japan..
                    kyoko-s@ka2.so-net.ne.jp
SOURCE:             Pancreas, (1999 Jul) Vol. 19, No. 1, pp. 98-104.
                    Journal code: 8608542. ISSN: 0885-3177.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        199908
ENTRY DATE:         Entered STN: 10 Sep 1999
                    Last Updated on STN: 10 Sep 1999
                    Entered Medline: 26 Aug 1999
AB   We have reported that cholecystokinin-like immunoreactivity (CCK-LI) and
     its transcripts are expressed in rat pancreatic islets (Endocrinology
```

1998;139:389-96). The purpose of this study was to elucidate the ontogeny of CCK during pancreatic development in the rat. Fetal rats from day 13 (E13) to 20 (E20) and postnatal (P) rats from day 1 to adulthood were used in this study. Immunohistochemical studies of rat pancreas were carried out with rabbit antisera against CCK-8 and gastrin-17. The absorption studies were performed by using CCK-8 antiserum incubated with excess CCK-8 or gastrin-17. In situ hybridization was performed to demonstrate the CCK and gastrin transcripts in the pancreas. CCK and gastrin were first detected at E15, and they were distributed in the periphery of the islets in the fetal and neonatal pancreas. The mirror sections for CCK revealed positive cells with characteristics identical to those that stained positive for gastrin. The CCK-LI in early development was completely abolished by preabsorption with excess gastrin but not with CCK-8. These findings indicated that the CCK-LI in the fetal and neonatal pancreas was crossreacting gastrin rather than CCK-8. From weaning (P21) through adulthood, on the other hand, CCK-LI was expressed diffusely in pancreatic islets, but there were no gastrin-positive cells after weaning. In situ hybridization showed that CCK messenger RNA (mRNA) was present in rat pancreatic islets in adults but not in early development. Although CCK-positive cells were not detected in fetal and neonatal pancreatic islets, CCK was expressed in islets during and after weaning through adulthood, indicating that CCK in pancreatic islets might be developmentally regulated.

L10 ANSWER 2 OF 25 MEDLINE on STN
ACCESSION NUMBER: 1998081791 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9421438
TITLE: Evidence for the existence of CCK-producing cells in rat pancreatic islets.
AUTHOR: Shimizu K; Kato Y; Shiratori K; Ding Y; Song Y; Furlanetto R; Chang T M; Watanabe S; Hayashi N; Kobayashi M; Chey W Y
CORPORATE SOURCE: Department of Gastroenterology, Tokyo Women's Medical College, Japan.
SOURCE: Endocrinology, (1998 Jan) Vol. 139, No. 1, pp. 389-96. Journal code: 0375040. ISSN: 0013-7227.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 29 Jan 1998
Last Updated on STN: 29 Jan 1998
Entered Medline: 15 Jan 1998

AB BACKGROUND: Although the existence of cholecystokinin-like immunoreactivity (CCK-LI) in rat pancreas had been reported previously, it was never clearly demonstrated whether CCK is produced in rat pancreatic islets. AIMS: The purpose of this study was to elucidate the source of the CCK-LI, the molecular properties of CCK, and the expression of the CCK gene in islet cells. METHODS: Immunohistochemical studies of rat pancreas were carried out with different rabbit antisera against CCK-8 and CCK-related peptide including N-terminal CCK-33 (1-22) and gastrin-17, and colocalization with known islet hormones including insulin, glucagon, somatostatin, and pancreatic polypeptide was investigated. The major molecular form of CCK in the islets was determined by HPLC. RT-PCR and in situ hybridization were performed to demonstrate the presence of the CCK transcript in the pancreas. RESULTS: CCK-LI was found in the center of the islets, colocalized with insulin in B cells. The major molecular form of CCK in the islets was CCK-8. A 350-nucleotide fragment of PCR-amplified CCK cDNA was detected in the islet as well as the duodenum by RT-PCR. In situ hybridization showed that CCK messenger RNA was located in a large portion

of the islets, and this was consistent with the immunohistochemical findings. CONCLUSION: CCK messenger RNA and immunoreactivity are expressed in adult rat pancreatic islets, indicating that CCK-producing cells are present in adult rat islets.

L10 ANSWER 3 OF 25 MEDLINE on STN
ACCESSION NUMBER: 86108879 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3943612
TITLE: Complete tyrosine O-sulfation of gastrin in adult and neonatal cat pancreas.
AUTHOR: Cantor P; Andersen B N; Rehfeld J F
SOURCE: FEBS letters, (1986 Jan 20) Vol. 195, No. 1-2, pp. 272-4. Journal code: 0155157. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198603
ENTRY DATE: Entered STN: 21 Mar 1990
Last Updated on STN: 21 Mar 1990
Entered Medline: 6 Mar 1986
AB We have found gastrin in both the adult and neonatal cat pancreas. In contrast with the main production sites, antrum and duodenum, gastrin in the pancreas occurs in a single molecular form, tyrosine O-sulfated gastrin-17. Since tyrosine sulfation increases the pancreozymic effect of gastrin, the complete sulfation seems functionally expedient.

L10 ANSWER 4 OF 25 MEDLINE on STN
ACCESSION NUMBER: 85217438 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4001448
TITLE: Complete sulfation of jejunal gastrin in the human fetus.
AUTHOR: Andersen B N; Abramovich D; Brand S J; Petersen B; Rehfeld J F
SOURCE: Regulatory peptides, (1985 Apr) Vol. 10, No. 4, pp. 329-38. Journal code: 8100479. ISSN: 0167-0115.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: (COMPARATIVE STUDY)
(IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198507
ENTRY DATE: Entered STN: 20 Mar 1990
Last Updated on STN: 20 Mar 1990
Entered Medline: 9 Jul 1985
AB The degree of tyrosine-O-sulfation and the ratio between large (gastrin-34 and component I) and small (gastrin-17 and -14) molecular forms of gastrin were studied in extracts of human fetal (n = 14) and adult (n = 9) antrum, duodenum, jejunum and pancreas. Boiled water extracts were applied to gel- and ion-exchange chromatography before and after treatment with trypsin and arylsulfatase. The fractions were monitored with sequence-specific radioimmunoassays that distinguish sulfated from non-sulfated gastrins. In antrum and duodenum about half the gastrins were sulfated at all stages of development. In the fetal jejunum gastrin occurred in sulfated form only while in the adult 72% (range, 64-88%) of the jejunal gastrins were sulfated. The larger molecular forms of gastrin predominated in the fetal compared with the adult antrum. In duodenum and jejunum, however, the ratio between small and large forms was the same in fetus and adult. Gastrin was undetectable

in both fetal and adult pancreas. The results show that the degree of sulfation of gastrin varies substantially in the different parts of the gut at different stages of development. The differences may have functional significance, since sulfation increases the pancreozyminic and cholecystokinetic potency of gastrin.

L10 ANSWER 5 OF 25 MEDLINE on STN
ACCESSION NUMBER: 80151120 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6987897
TITLE: Secretory effects of gastrins on isolated perfused porcine pancreas.
AUTHOR: Jensen S L; Rehfeld J F; Holst J J; Fahrenkrug J; Nielsen O V; Schaffalitzky de Muckadell O B
SOURCE: The American journal of physiology, (1980 Feb) Vol. 238, No. 2, pp. E186-92.
Journal code: 0370511. ISSN: 0002-9513.
PUB. COUNTRY: United States
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198005
ENTRY DATE: Entered STN: 15 Mar 1990
Last Updated on STN: 15 Mar 1990
Entered Medline: 14 May 1980
AB The effects of the four main forms of gastrin (component I, gastrin-34, gastrin-17, and gastrin-14) on insulin, glucagon, and exocrine secretion were measured on the isolated perfused porcine pancreas. All gastrins were studied in concentrations ranging from 10(-11) to 10(-8) M. Depending on the glucose concentration in the perfusate, all four gastrins increased insulin or glucagon secretion in a dose-dependent manner in concentrations above 10(-10) M. These concentrations are slightly above the arterial concentrations in normal pig and man, but they correspond to gastrin concentrations measured in patients with achlorhydria and gastrinomas. The exocrine secretion was stimulated by all gastrins in a dose-dependent manner. The lowest concentrations that stimulated flow rate significantly were within the physiologic range, 10(-11) and 10(-10) M. All gastrins induced maximal flow rate at a concentration of 10(-9) M. The sulfated form of gastrin-17 had the greatest efficacy. The results indicate that all gastrins may influence the exocrine secretion under normal conditions and the endocrine secretion in diseases with endogenous hypergastrinemia.

L10 ANSWER 6 OF 25 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 1999:370619 BIOSIS
DOCUMENT NUMBER: PREV199900370619
TITLE: Expression of cholecystokinin in the pancreas during development.
AUTHOR(S): Shimizu, K. [Reprint author]; Shiratori, K.; Sakayori, N.; Kobayashi, M.; Hayashi, N.
CORPORATE SOURCE: Department of Gastroenterology and Clinical Laboratory, School of Medicine, Tokyo Women's Medical University, 8-1, Kawada-cho, Shinjuku-ku, Tokyo, 162, Japan
SOURCE: Pancreas, (July, 1999) Vol. 19, No. 1, pp. 98-104. print.
CODEN: PANCE4. ISSN: 0885-3177.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Sep 1999
Last Updated on STN: 9 Sep 1999
AB We have reported that cholecystokinin-like immunoreactivity (CCK-LI) and its transcripts are expressed in rat pancreatic islets (Endocrinology 1998;139:389-96). The purpose of this study was to elucidate the ontogeny

of CCK during pancreatic development in the rat. Fetal rats from day 13 (E13) to 20 (E20) and postnatal (P) rats from day 1 to adulthood were used in this study. Immunohistochemical studies of rat pancreas were carried out with rabbit antisera against CCK-8 and gastrin-17. The absorption studies were performed by using CCK-8 antiserum incubated with excess CCK-8 or gastrin-17. In situ hybridization was performed to demonstrate the CCK and gastrin transcripts in the pancreas. CCK and gastrin were first detected at E15, and they were distributed in the periphery of the islets in the fetal and neonatal pancreas. The mirror sections for CCK revealed positive cells with characteristics identical to those that stained positive for gastrin. The CCK-LI in early development was completely abolished by preabsorption with excess gastrin but not with CCK-8. These findings indicated that the CCK-LI in the fetal and neonatal pancreas was crossreacting gastrin rather than CCK-8. From weaning (P21) through adulthood, on the other hand, CCK-LI was expressed diffusely in pancreatic islets, but there were no gastrin-positive cells after weaning. In situ hybridization showed that CCK messenger RNA (mRNA) was present in rat pancreatic islets in adults but not in early development. Although CCK- positive cells were not detected in fetal and neonatal pancreatic islets, CCK was expressed in islets during and after weaning through adulthood, indicating that CCK in pancreatic islets might be developmentally regulated.

L10 ANSWER 7 OF 25 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 1998:74975 BIOSIS
DOCUMENT NUMBER: PREV199800074975
TITLE: Evidence for the existence of CCK-producing cells in rat pancreatic islets.
AUTHOR(S): Shimizu, K. [Reprint author]; Kato, Y.; Shiratori, K.; Ding, Y.; Song, Y.; Furlanetto, R.; Chang, T.-M.; Watanabe, S.; Hayashi, N.; Kobayashi, M.; Chey, W. Y.
CORPORATE SOURCE: Tokyo Women's Med. Coll., Dep. Gastroenterol., 8-1 Kawada-cho, Shinjuku-Ku, Tokyo 162, Japan
SOURCE: Endocrinology, (Jan., 1998) Vol. 139, No. 1, pp. 389-396. print.
CODEN: ENDOAO. ISSN: 0013-7227.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Feb 1998
Last Updated on STN: 24 Feb 1998

AB Background: Although the existence of cholecystokinin-like immunoreactivity (CCK-LI) in rat pancreas had been reported previously, it was never clearly demonstrated whether CCK is produced in rat pancreatic islets. Aims: The purpose of this study was to elucidate the source of the CCK-LI, the molecular properties of CCK, and the expression of the CCK gene in islet cells. Methods: Immunohistochemical studies of rat pancreas were carried out with different rabbit antisera against CCK-8 and CCK-related peptide including N-terminal CCK-33 (1-22) and gastrin-17, and colocalization with known islet hormones including insulin, glucagon, somatostatin, and pancreatic polypeptide was investigated. The major molecular form of CCK in the islets was determined by HPLC. RT-PCR and in situ hybridization were performed to demonstrate the presence of the CCK transcript in the pancreas. Results: CCK-LI was found in the center of the islets, colocalized with insulin in B cells. The major molecular form of CCK in the islets was CCK-8. A 350-nucleotide fragment of PCR-amplified CCK cDNA was detected in the islet as well as the duodenum by RT-PCR. In situ hybridization showed that CCK messenger RNA was located in a large portion of the islets, and this was consistent with the immunohistochemical findings. Conclusion: CCK messenger RNA and immunoreactivity are expressed in adult rat pancreatic islets, indicating that CCK-producing cells are present in adult rat islets.

L10 ANSWER 8 OF 25 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 1985:360332 BIOSIS
DOCUMENT NUMBER: PREV198580030324; BA80:30324
TITLE: COMPLETE SULFATION OF JEJUNAL GASTRIN IN THE HUMAN FETUS.
AUTHOR(S): ANDERSEN B N [Reprint author]; ABRAMOVICH D; BRAND S J; PETERSEN B; REHFELD J F
CORPORATE SOURCE: DEP CLINICAL CHEM, RIGSHOSPITALET, BLEGDAMSVEJ 9, DK-2100 COPENHAGEN, DENMARK
SOURCE: Regulatory Peptides, (1985) Vol. 10, No. 4, pp. 329-338. CODEN: REPPDY. ISSN: 0167-0115.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
AB The degree of tyrosine-O-sulfation and the ratio between large (gastrin-34 and component I) and small (gastrin-17 and -14) molecular forms of gastrin were studied in extracts of human fetal (n = 14) and adult (n = 9) antrum, duodenum, jejunum and pancreas. Boiled water extracts were applied to gel- and ion-exchange chromatography before and after treatment with trypsin and arylsulfatase. The fractions were monitored with sequence-specific radioimmunoassays that distinguish sulfated from non-sulfated gastrins. In antrum and duodenum about half the gastrins were sulfated at all stages of development. In the fetal jejunum gastrin occurred in sulfated form only while in the adult 72% (range, 64-88%) of the jejunal gastrins were sulfated. The larger molecular forms of gastrin predominated in the fetal compared with the adult antrum. In duodenum and jejunum, the ratio between small and large forms was the same in fetus and adult. Gastrin was undetectable in both fetal and adult pancreas. The degree of sulfation of gastrin varies substantially in the different parts of the gut at different stages of development. The differences may have functional significance, since sulfation increases the pancreozyminic and cholecystokinetic potency of gastrin.

L10 ANSWER 9 OF 25 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 1980:202572 BIOSIS
DOCUMENT NUMBER: PREV198069077568; BA69:77568
TITLE: SECRETORY EFFECTS OF GASTRINS ON ISOLATED PERFUSED PORCINE PANCREAS.
AUTHOR(S): JENSEN S L [Reprint author]; REHFELD J F; HOLST J J; FAHRENKRUG J; NIELSEN O V; SCHAFFALITZKY DE MUCKADELL O B
CORPORATE SOURCE: DEP SURG GASTROENTEROL C, RIGSHOSP, UNIV COPENH, DK-2100 COPENHAGEN O, DEN
SOURCE: American Journal of Physiology, (1980) Vol. 238, No. 2, pp. E186-E192. CODEN: AJPHAP. ISSN: 0002-9513.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
AB The effects of the 4 main forms of gastrin (component I, gastrin-34, gastrin-17 and gastrin-14) on insulin, glucagon and exocrine secretion were measured on the isolated perfused porcine pancreas. All gastrins were studied in concentrations ranging from 10-11-10-8 M. Depending on the glucose concentration in the perfusate, all 4 gastrins increased insulin or glucagon secretion in a dose-dependent manner in concentrations above 10-10 M. These concentrations are slightly above the arterial concentrations in normal pig and man, but they correspond to gastrin concentrations measured in patients with achlorhydria and gastrinomas. The exocrine secretion was stimulated by all gastrins in a dose-dependent manner. The lowest concentrations that stimulated flow rate significantly were within the physiologic range, 10-11 and 10-10 M. All gastrins induced maximal flow

rate at a concentration of 10-9 M. The sulfated form of gastrin-17 had the greatest efficacy. All gastrins may influence the exocrine secretion under normal conditions and the endocrine secretion in diseases with endogenous hypergastrinemia.

L10 ANSWER 10 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1055900 CAPLUS
DOCUMENT NUMBER: 143:360319
TITLE: Reduced ghrelin, islet amyloid polypeptide, and peptide YY expression in the stomach of gastrin-cholecystokinin knockout mice
AUTHOR(S): Friis-Hansen, Lennart; Wierup, Nils; Rehfeld, Jens F.; Sundler, Frank
CORPORATE SOURCE: Department of Clinical Biochemistry, Rigshospitalet, University of Copenhagen, Copenhagen, DK-2100, Den.
SOURCE: Endocrinology (2005), 146(10), 4464-4471
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The antral hormone gastrin and its intestinal relative, cholecystokinin (CCK), are pivotal in the regulation of gastric functions. Other gastric hormones like ghrelin, peptide YY (PYY), and islet amyloid polypeptide (IAPP), however, also contribute to the regulation of acid secretion, motility, and feeding. Because gastrin and CCK are crucial for gastric homeostasis, the authors examined how loss of gastrin alone and gastrin plus CCK affected the expression of ghrelin, IAPP, and PYY and ghrelin secretion. The expression of ghrelin, IAPP, and PYY and the CCK-A receptor genes were examined in both gastrin and gastrin-CCK double-knockout (KO) mice using immunocytochem. and quant. RT-PCR. Ghrelin concns. in plasma were measured using RIA. Gastrin and CCK were infused in gastrin-CCK KO mice using osmotic minipumps. The number of ghrelin cells and ghrelin gene expression were unaffected, albeit the ghrelin cells were located closer to the base of the glands in both KO mouse strains when freely fed. However, lack of both gastrin and CCK attenuated fasting-induced ghrelin expression and secretion. Fundic ghrelin cells expressed the CCK-A receptor, and ghrelin expression increased after CCK infusion. Furthermore, gastric IAPP and PYY expression as well as the number of IAPP- and PYY-containing cells were reduced in both gastrin and gastrin-CCK KO mice. Gastrin infusion increased gastric IAPP but not PYY expression. In conclusion, lack of gastrin plus CCK but not gastrin alone reduced ghrelin secretion in response to fasting through both direct and indirect mechanisms. Both gastrin and combined gastrin-CCK deficiency reduced the gastric IAPP and PYY expression.
REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:368884 CAPLUS
DOCUMENT NUMBER: 140:386447
TITLE: Methods and composition for the treatment of diabetes with FACGINT (FActor for Complementing Gastrin for Islet Neogenesis Therapy)
INVENTOR(S): Brand, Stephen J.; Cruz, Antonio; Pastrak, Aleksandra; Hew, Yin
PATENT ASSIGNEE(S): Waratah Pharmaceuticals, Inc., Can.
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004037195	A2	20040506	WO 2003-US33595	20031022
WO 2004037195	A3	20050616		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2501677	A1	20040506	CA 2003-2501677	20031022
AU 2003283004	A1	20040513	AU 2003-283004	20031022
BR 2003015523	A	20050830	BR 2003-15523	20031022
EP 1569680	A2	20050907	EP 2003-774936	20031022
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1729016	A	20060201	CN 2003-80107284	20031022
JP 2006506386	T	20060223	JP 2004-547077	20031022
EP 1884247	A2	20080206	EP 2007-19263	20031121
EP 1884247	A3	20080213		
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PT, RO, SE, SI, SK, TR				
MX 2005PA04202	A	20050920	MX 2005-PA4202	20050420
IN 2005KN00910	A	20060623	IN 2005-KN910	20050517
NO 2005002419	A	20050707	NO 2005-2419	20050519
US 20060189520	A1	20060824	US 2006-532295	20060217
PRIORITY APPLN. INFO.:			US 2002-420187P	P 20021022
			US 2002-420399P	P 20021022
			US 2002-428100P	P 20021121
			US 2002-428562P	P 20021122
			US 2002-430590P	P 20021203
			WO 2003-US33595	W 20031022
			US 2003-519933P	P 20031114
			EP 2003-778179	A3 20031121

AB Compns. and methods are provided for islet neogenesis therapy comprising a member of a group of factors that complement a gastrin/CCK receptor ligand, with formulations, devices and methods for sustained release delivery and for local delivery to target organs. Methods and composition for the transplantation of stem cells and stimulation to proliferate and differentiated into insulin-producing cells are also claimed.

L10 ANSWER 12 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:854664 CAPLUS

DOCUMENT NUMBER: 140:139796

TITLE: Hypoglycemia, defective islet glucagon secretion, but normal islet mass in mice with a disruption of the gastrin gene

AUTHOR(S): Boushey, Robin P.; Abadir, Amir; Flamez, Daisy; Baggio, Laurie L.; Li, Yazhou; Berger, Veerle; Marshall, Bess A.; Finegood, Diane; Wang, Timothy C.; Schuit, Frans; Drucker, Daniel J.

CORPORATE SOURCE: Department of Medicine, Banting and Best Diabetes Centre, Toronto General Hospital, University of Toronto, Toronto, ON, Can.

SOURCE: Gastroenterology (2003), 125(4), 1164-1174
CODEN: GASTAB; ISSN: 0016-5085

PUBLISHER: W. B. Saunders Co.

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Both cholecystokinin (CCK)-A and CCK-B receptors are expressed in the pancreas, and exogenous gastrin administration stimulates glucagon secretion from human islets. Although gastrin action has been linked to islet neogenesis, transdifferentiation, and beta-cell regeneration, an essential physiol. role(s) for gastrin in the pancreas has not been established. The authors examined glucose homeostasis, glucagon gene expression, glucagon secretion, and islet mass in mice with a targeted gastrin gene disruption. Gastrin -/- mice exhibit fasting hypoglycemia and significantly reduced glycemic excursion following glucose challenge. Insulin sensitivity was normal and levels of circulating insulin and insulin mRNA transcripts were appropriately reduced in gastrin -/- mice. In contrast, levels of circulating glucagon and pancreatic glucagon mRNA transcripts were not up-regulated in hypoglycemic gastrin -/- mice. Furthermore, the glucagon response to epinephrine in isolated perifused islets was moderately impaired in gastrin -/- vs. gastrin +/+ islets (40% reduction;, gastrin +/+ vs. gastrin -/- mice). Moreover, the glucagon response but not the epinephrine response to hypoglycemia was significantly attenuated in gastrin -/- compared with gastrin +/+ mice. Despite gastrin expression in the developing fetal pancreas, beta-cell area, islet topog., and the islet proliferative response to exptl. injury were normal in gastrin -/- mice. These findings show an essential physiol. role for gastrin in glucose homeostasis; however, the gastrin gene is not essential for murine islet development or the adaptive islet proliferative response to beta-cell injury.
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 13 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:690470 CAPLUS
DOCUMENT NUMBER: 140:13276
TITLE: Receptor subtypes: species variations in secretin affect potency for pancreatic but not gastric secretion
AUTHOR(S): Solomon, Travis E.; Keire, David A.; Gong, Peixian; Zong, Yumei; Reeve, Joseph R., Jr.
CORPORATE SOURCE: CURE Digestive Diseases Research Center, VA Greater Los Angeles Healthcare System, UCLA School of Medicine, Los Angeles, CA, USA
SOURCE: Pancreas (Hagerstown, MD, United States) (2003), 26(3), 300-305
CODEN: PANCE4; ISSN: 0885-3177
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Introduction: Receptor subtypes can be distinguished by different actions of agonists on physiol. responses. In this study, we compared effects of four species variants of secretin (rat, porcine, canine, and human) on pancreatic secretion and gastrin-induced acid secretion in urethane-anesthetized rats. These secretins differ by one to three residues in position 14, 15, or 16 and were used to probe for the presence of different secretin receptor subtypes in the rat. Methodol.: Pancreatic responses were measured in a two-point parallel line bioassay with porcine secretin (3 and 30 pmol/kg IV bolus) as standard Inhibition of gastric acid secretion by each secretin (100 pmol/[kg · h]) was quantitated against a threshold dosage of gastrin-17 (200 pmol/[kg · h]), and percent inhibition of incremental acid responses was determined Results: Rat secretin was significantly more potent than other secretins for pancreatic secretion, in the order of rat > porcine > canine > human. The four secretins significantly inhibited gastrin-induced acid secretion by 37% to 49%, with no statistically significant differences among the forms.

Conclusions: Stimulation of pancreatic secretion was influenced by species variations in secretin structure, but inhibition of gastric acid secretion was not. This finding suggests that secretin receptor subtypes with different recognition patterns mediate these responses.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 14 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:758935 CAPLUS
DOCUMENT NUMBER: 139:34842
TITLE: Phase II study of anti-gastrin-17 antibodies, raised to G17DT, in advanced pancreatic cancer
AUTHOR(S): Brett, B. T.; Smith, S. C.; Bouvier, C. V.; Michaeli, D.; Hochhauser, D.; Davidson, B. R.; Kurzawinski, T. R.; Watkinson, A. F.; Van Someren, N.; Pounder, R. E.; Caplin, M. E.
CORPORATE SOURCE: Department of Medicine, Royal Free Hospital National Health Service Trust, London, UK
SOURCE: Journal of Clinical Oncology (2002), 20(20), 4225-4231
CODEN: JCONDN; ISSN: 0732-183X
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The prognosis for advanced pancreatic cancer remains poor. Gastrin acts as a growth factor for pancreatic cancer. We describe the first study of the antigastrin immunogen G17DT in pancreatic cancer. Our aims were to determine the antibody response, safety, tolerability, and preliminary evidence of efficacy of G17DT in advanced pancreatic cancer. Thirty patients with advanced pancreatic cancer were immunized with three doses of either 100 μg or 250 μg of G17DT. In the whole group, 20 (67%) of 30 patients produced an antibody response. The 250-μg dose resulted in a significantly greater response rate of 82% compared with 46% for the 100-μg group (P = .018). The most significant side effects, seen in three patients, were local abscess and/or fever. The median survival for the whole group from the date of the first immunization was 187 days; median survival was 217 days for the antibody responders and 121 days for the antibody nonresponders. The difference in survival between the antibody responders and nonresponders was significant (P = .0023). Patients with advanced pancreatic cancer are able to mount an adequate antibody response to G17DT. The 250-μg dose is superior to the 100-μg dose, and it appears to be generally well tolerated. Antibody responders demonstrate significantly greater survival than antibody nonresponders. Phase III studies are currently underway in order to determine efficacy.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 15 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:539568 CAPLUS
DOCUMENT NUMBER: 137:103902
TITLE: Prolonged efficacy of islet neogenesis therapy methods with a gastrin/CCK receptor ligand and an EGF receptor ligand composition in subjects with preexisting diabetes
INVENTOR(S): Brand, Stephen J.
PATENT ASSIGNEE(S): Waratah Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002055152	A2	20020718	WO 2002-US685	20020111
WO 2002055152	A9	20030123		
WO 2002055152	A3	20030410		
W: AU, CA, CN, HU, IL, IN, JP, KR, NO, PH, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
CA 2434330	A1	20020718	CA 2002-2434330	20020111
AU 2002243501	A1	20020724	AU 2002-243501	20020111
AU 2002243501	B2	20071122		
US 20020098178	A1	20020725	US 2002-44048	20020111
US 6992060	B2	20060131		
EP 1351742	A2	20031015	EP 2002-708990	20020111
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
JP 2004520345	T	20040708	JP 2002-555881	20020111
IN 2003KN00875	A	20050311	IN 2003-KN875	20030708
ZA 2003005347	A	20041011	ZA 2003-5347	20030710
US 20060234932	A1	20061019	US 2005-273615	20051114
PRIORITY APPLN. INFO.:			US 2001-261638P	P 20010112
			US 2002-44048	A1 20020111
			WO 2002-US685	W 20020111

AB Compns. and methods are provided for achieving in vivo islet cell regeneration in subjects with preexisting diabetes. The methods comprise short term treatment with a composition having a gastrin/cholecystokinin receptor ligand and an EGF receptor ligand. Treatment with such a composition for a short term resulted in a prolonged period of increased insulin release, decreased fasting blood glucose, and improved glucose tolerance, the prolonged efficacy, the period being considered from the time of cessation of treatment.

L10 ANSWER 16 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:12267 CAPLUS
DOCUMENT NUMBER: 128:123967
TITLE: Evidence for the existence of CCK-producing cells in rat pancreatic islets
AUTHOR(S): Shimizu, K.; Kato, Y.; Shiratori, K.; Ding, Y.; Song, Y.; Furlanetto, R.; Chang, T.-M.; Watanabe, S.; Hayashi, N.; Kobayashi, M.; Chey, W. Y.
CORPORATE SOURCE: Dep. Gastroenterology, Tokyo Women's Med. College, Tokyo, 162, Japan
SOURCE: Endocrinology (1998), 139(1), 389-396
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Although the existence of cholecystokinin-like immunoreactivity (CCK-LI) in rat pancreas had been reported previously, it was never clearly demonstrated whether CCK is produced in rat pancreatic islets. The purpose of this study was to elucidate the source of the CCK-LI, the mol. properties of CCK, and the expression of the CCK gene in islet cells. Immunohistochem. studies of rat pancreas were carried out with different rabbit antisera against CCK-8 and CCK-related peptide including N-terminal CCK-33 (1-22) and gastrin-17, and colocalization with known islet hormones including insulin, glucagon, somatostatin, and pancreatic polypeptide was investigated. The major mol. form of CCK in the islets was determined by HPLC. RT-PCR and in situ hybridization were performed to demonstrate the presence of the CCK transcript in the pancreas. CCK-LI was found in the center of the islets, colocalized with insulin in B cells. The major mol. form of CCK in the

islets was CCK-8. A 350-nucleotide fragment of PCR-amplified CCK cDNA was detected in the islet as well as the duodenum by RT-PCR. In situ hybridization showed that CCK mRNA was located in a large portion of the islets, and this was consistent with the immunohistochem. findings. CCK mRNA and immunoreactivity are expressed in adult rat pancreatic islets, indicating that CCK-producing cells are present in adult rat islets.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> S Structure(S)(Gastrin-17 OR Gastrin 17 OR Gastrin I)
L1   47 STRUCTURE(S)(GASTRIN-17 OR GASTRIN 17 OR GASTRIN I)

=> Dup Rem L1
PROCESSING COMPLETED FOR L1
L2   28 DUP REM L1 (19 DUPLICATES REMOVED)
               ANSWERS '1-8' FROM FILE MEDLINE
               ANSWERS '9-10' FROM FILE BIOSIS
               ANSWERS '11-27' FROM FILE CAPLUS
               ANSWER '28' FROM FILE EMBASE

=> D TI L2 1-28

L2   ANSWER 1 OF 28   MEDLINE on STN   DUPLICATE 1
TI   Naming progastrin-derived peptides.

L2   ANSWER 2 OF 28   MEDLINE on STN   DUPLICATE 2
TI   Ferric ions are essential for the biological activity of the hormone
     glycine-extended gastrin.

L2   ANSWER 3 OF 28   MEDLINE on STN   DUPLICATE 3
TI   Purification and structural characterization of progastrin-derived
     peptides from a human gastrinoma.

L2   ANSWER 4 OF 28   MEDLINE on STN   DUPLICATE 4
TI   [Synthesis of peptides with gastrinlike activity. Studies on the
     structure-activity relationship of the natural hormone human
     little gastrin I].
     Synthese von Gastrin-aktiven Peptiden. Untersuchungen zur
     Struktur-Wirkungsbeziehung des naturlichen Hormons Human-Little-Gastrin-I.

L2 ANSWER 5 OF 28 MEDLINE on STN DUPLICATE 6
TI [Cholecystokinin-pancreozymin synthesis. Synthesis of [28-threonine,31-norleucine]- and [28-threonine,31-leucine]cholecystokinin-pancreozymin-(25-33)-nonapeptide].
Zur Synthese von Cholecystokinin-Pankreozymin. Darstellung von [28-Threonin,31-Norleucin]- und [28-Threonin,31-Leucin]Cholecystokinin-Pankreozymin-(25-33)-nonapeptid.

L2 ANSWER 6 OF 28 MEDLINE on STN DUPLICATE 7
TI [Total synthesis of human big gastrin I. Revised primary structure (author's transl)].
Totalsynthese des Human-Big-Gastrins I. Revidierte Primarstruktur.

L2 ANSWER 7 OF 28 MEDLINE on STN DUPLICATE 9
TI Structures of human gastrins I and II.

L2 ANSWER 8 OF 28 MEDLINE on STN
TI [Total synthesis of human big gastrin I and the 32-leucine analogue (author's transl)].
Zur Totalsynthese des Human-Big-Gastrins I und seines 32-Leucin-Analogons.

L2 ANSWER 9 OF 28 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 8
TI A NEW TYPE OF GASTRIN DERIVATIVE AND ITS USE FOR PRODUCTION OF CENTRAL REGION SPECIFIC ANTI GASTRIN SERA.

L2 ANSWER 10 OF 28 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI TOTAL SYNTHESIS OF HUMAN BIG GASTRIN I AND THE 32 LEUCINE ANALOG PRELIMINARY COMMUNICATION.

L2 ANSWER 11 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 5
TI Synthesis of big gastrin I (human). Part 5. Total synthesis of the sequence-revised tetratriacontapeptide amide

L2 ANSWER 12 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
TI Contribution of C-terminal structures of gastrin to receptor recognition

L2 ANSWER 13 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
TI Partial agonism by gastrin for a cholecystokinin receptor mediating pepsinogen secretion

L2 ANSWER 14 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
TI Identification of four chicken gastrins, obtained by processing at post-Phe bonds

L2 ANSWER 15 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
TI Importance of sulfation of gastrin or cholecystokinin (CCK) on affinity for gastrin and CCK receptors

L2 ANSWER 16 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
TI The effects of various gastrins on intracellular free calcium in isolated pig parietal cells

L2 ANSWER 17 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
TI Binding of gastrin17 to human gastric carcinoma cell lines

L2 ANSWER 18 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
TI Structure-activity studies of C- and N-terminal fragments of cholecystokinin 26-33 in guinea pig isolated tissues

L2 ANSWER 19 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
TI Similar acid stimulatory potencies of synthetic human big and little gastrins in man

L2 ANSWER 20 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
TI Antibodies to gastrin

L2 ANSWER 21 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
TI Feline gastrin. An example of peptide sequence analysis by mass spectrometry

L2 ANSWER 22 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
TI Structure and synthesis of canine gastrin

L2 ANSWER 23 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
TI Gastrins from some mammalian species

L2 ANSWER 24 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
TI Human gastrin: isolation, structure, and synthesis. Synthesis of human gastrin I

L2 ANSWER 25 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
TI Gastrin: Structure and synthesis

L2 ANSWER 26 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
TI Synthesis of peptides related to gastrin

L2 ANSWER 27 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
TI Antral hormone gastrin. Structure of gastrin

L2 ANSWER 28 OF 28 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
TI Identification of a 70-kDa gastrin-binding protein on DLD-1 human colorectal carcinoma cells.

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FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 09:51:57 ON 04 APR 2008
L1 47 S STRUCTURE(S)(GASTRIN-17 OR GASTRIN 17 OR GASTRIN I)
L2 28 DUP REM L1 (19 DUPLICATES REMOVED)

=> D IBIB abs L2 1,3,4,6,7,10,12,13,17,18,21,22,24-26

L2 ANSWER 1 OF 28 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2004279538 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15177936
TITLE: Naming progastrin-derived peptides.
AUTHOR: Rehfeld Jens F; Bundgaard Jens R; Goetze Jens P; Friis-Hansen Lennart; Hilsted Linda; Johnsen Anders H
CORPORATE SOURCE: Department of Clinical Biochemistry (KB 3014), Rigshospitalet, University of Copenhagen, DK-2100, Denmark.. rehfeld@rh.dk
SOURCE: Regulatory peptides, (2004 Aug 15) Vol. 120, No. 1-3, pp. 177-83. Ref: 38
Journal code: 8100479. ISSN: 0167-0115.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200501
ENTRY DATE: Entered STN: 6 Jun 2004
Last Updated on STN: 12 Jan 2005
Entered Medline: 11 Jan 2005

AB The antral hormone gastrin continues to be in focus, because its hormonal and growth promoting effects are essential both for the function of the normal stomach and for the pathogenesis of major dyspeptic and neoplastic diseases. Deduction of the progastrin structure has improved the insight in the cellular synthesis of gastrin, but has also revealed that the biosynthetic machinery is complex, and, accordingly, that progastrin is processed to a multitude of more or less bioactive fragments. The naming of these fragments has, however, become inconsistent and confusing. Therefore, we propose a systematic nomenclature for progastrin-derived peptides of which there are three classes: (I) The gastrins with the evolutionary preserved tetrapeptide amide (Trp-Met-Asp-PheNH2) at the C-terminus, which ensures high-affinity binding to the gastrin (CCK-B) receptor. Among the gastrins, gastrin-34 and gastrin-17 constitute the primary forms. (II) Processing intermediates, which are early products of progastrin that contain the structure of the primary gastrins within their sequence, but still cannot bind the gastrin receptor due to insufficient processing at their C-terminus. (III) Flanking fragments from the N- and C-termini of progastrin that do not contain any primary gastrin in their sequence, but nevertheless may undergo posttranslational processing. Each fragment can be specified with suffixes corresponding to the derived sequence in progastrin.

L2 ANSWER 3 OF 28 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 91286236 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2061307
TITLE: Purification and structural characterization of progastrin-derived peptides from a human gastrinoma.
AUTHOR: Huebner V D; Jiang R L; Lee T D; Legesse K; Walsh J H;

Shively J E; Chew P; Azumi T; Reeve J R Jr
CORPORATE SOURCE: Beckman Research Institute of the City of Hope, Duarte, California 91010.
CONTRACT NUMBER: DK17294 (United States NIDDK)
DK17328 (United States NIDDK)
DK33850 (United States NIDDK)
+
SOURCE: The Journal of biological chemistry, (1991 Jul 5) Vol. 266, No. 19, pp. 12223-7.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199108
ENTRY DATE: Entered STN: 25 Aug 1991
Last Updated on STN: 3 Mar 2000
Entered Medline: 7 Aug 1991

AB Several peptides derived from the gastrin-predicted preprohormone sequence were isolated from a human gastrinoma by gel permeation, anion exchange, and reverse phase chromatography. The peptides were identified and characterized structurally by a combination of radioimmunoassays, mass spectral analysis, and microsequence analysis. The largest peptide, progastrin-(1-35) (cryptagastrin), extends from the putative processing site for the signal peptidase to the double basic residues adjacent to the amino terminus of gastrin 34. A shorter form of this peptide, progastrin-(6-35) (cryptagastrin-(6-35), was also isolated in smaller amounts. In addition, sulfated and nonsulfated gastrin 17 amides (progastrin-(55-71)) and the glycine-extended nonsulfated gastrin 17 (progastrin-(55-72)) were identified by radioimmunoassay, and their structures were confirmed by mass spectral analysis. Isolation of cryptagastrin indicates that the signal peptide of human preprogastrin contains 21 amino acid residues, and progastrin, therefore, contains 80 amino acids. There is minimal processing of the cryptic peptide preceding the sequence of gastrin 34. An amidated gastrin form larger than gastrin 34 could contain 71 amino acids. No evidence was obtained for processing that would produce gastrins containing more than 34 but less than 71 amino acid residues.

L2 ANSWER 4 OF 28 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 84184194 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6714937
TITLE: [Synthesis of peptides with gastrinlike activity. Studies on the structure-activity relationship of the natural hormone human little gastrin I
].
Synthese von Gastrin-aktiven Peptiden. Untersuchungen zur Struktur-Wirkungsbeziehung des naturlichen Hormons Human-Little-Gastrin-I.
AUTHOR: Gohring W; Moroder L; Borin G; Lobbia A; Bali J P; Wunsch E
SOURCE: Hoppe-Seyler's Zeitschrift fur physiologische Chemie, (1984 Jan) Vol. 365, No. 1, pp. 83-94.
Journal code: 2985060R. ISSN: 0018-4888.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198406

ENTRY DATE: Entered STN: 19 Mar 1990
Last Updated on STN: 19 Mar 1990
Entered Medline: 6 Jun 1984

AB To identify the role of the block of glutamic acid residues characteristic for the gastrin molecule, a series of shortened peptides related to the human little-gastrin-I sequence were synthesized. The biological activities of these gastrin peptides strongly suggest in the pentaglutamic acid sequence a specific information for a pronounced amplification of the hormonal activity.

L2 ANSWER 6 OF 28 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 81166271 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6783501
TITLE: [Total synthesis of human big gastrin I
. Revised primary structure (author's transl)].
Totalsynthese des Human-Big-Gastrins I. Revidierte
Primarstruktur.
AUTHOR: Wunsch E; Wendlberger G; Mladenova-Orlinova L; Gohring W;
Jaeger E; Scharf R
SOURCE: Hoppe-Seyler's Zeitschrift fur physiologische Chemie, (1981
Feb) Vol. 362, No. 2, pp. 179-83.
Journal code: 2985060R. ISSN: 0018-4888.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198106
ENTRY DATE: Entered STN: 16 Mar 1990
Last Updated on STN: 16 Mar 1990
Entered Medline: 13 Jun 1981

AB The synthesis of the tetratriacontapeptide amide corresponding to the revised structure of human big gastrin I is described. The fully protected peptide derivative was obtained by assembly in sequence order of the suitably protected fragments [1--9], [10--14] and [15--34] via the dicyclohexylcarbodiimide/N-hydroxysuccinimide and azide method, respectively. Upon removal of the protecting groups by exposure to trifluoroacetic acid and purification of the resulting crude product by chromatographic methods, human big gastrin I was obtained in satisfactory yields and at a high degree of purity. The identical immunological crossreactivities of natural and synthetic human big gastrin I using anti-porcine big gastrin
I antiserum strongly supports the correctness of the newly proposed primary structure of this member of the gastrin family.

L2 ANSWER 7 OF 28 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 67021327 MEDLINE
DOCUMENT NUMBER: PubMed ID: 5921183
TITLE: Structures of human gastrins I
and II.
AUTHOR: Bentley P H; Kenner G W; Sheppard R C
SOURCE: Nature, (1966 Feb 5) Vol. 209, No. 5023, pp. 583-5.
Journal code: 0410462. ISSN: 0028-0836.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 196701
ENTRY DATE: Entered STN: 1 Jan 1990
Last Updated on STN: 1 Jan 1990
Entered Medline: 8 Jan 1967

L2 ANSWER 10 OF 28 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 1978:129673 BIOSIS
DOCUMENT NUMBER: PREV197865016673; BA65:16673
TITLE: TOTAL SYNTHESIS OF HUMAN BIG GASTRIN I AND THE 32 LEUCINE ANALOG PRELIMINARY COMMUNICATION.
AUTHOR(S): WUENSCH E [Reprint author]; WENDLBERGER G; HALLETT A; JAEGER E; KNOF S; MORODER L; SCHARF R; SCHMIDT I; THAMM P; ET AL
CORPORATE SOURCE: MAX-PLANCK-INST BIOCHEM, ABT PEPTIDCHEM, D-8033 MARTINSRIED MUENCHEN, W GER
SOURCE: Zeitschrift fuer Naturforschung Section C Journal of Biosciences, (1977) Vol. 32, No. 7-8, pp. 495-506. ISSN: 0939-5075.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: GERMAN
AB A new total synthesis of the tetratriacontapeptide amide corresponding to the proposed primary structure of human big gastrin I is described. The synthetic route was based on the preparation of 6 suitably protected fragments, related to sequence 28-34, 23-27, 21-22, 15-20, 9-14 and 1-8, to be used as building blocks for total synthesis. Protecting groups were selected according to the Schwyzer-Wuensch strategy of maximum side chain protection based on tertiary alcohols, also for the imidazol function of histidine. Subsequent assembly of the 6 fragments by 3 different pathways was performed using the highly efficient Wuensch-Weygand condensation procedure to ensure minimum racemization. This was followed by deprotection of synthetic products via exposure to trifluoroacetic acid and final purification by ion-exchange chromatography on DEAE-Sephadex A-25 and partition chromatography on Sephadex G-25, which led to human big gastrin I, homogeneous within limits of analytical methods used. Biological activity of the synthetic product proved to be 50% higher than that of human little gastrin I. The 32-leucine analogue of human big gastrin I was prepared in the same way.

L2 ANSWER 12 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:509412 CAPLUS
DOCUMENT NUMBER: 140:175297
TITLE: Contribution of C-terminal structures of gastrin to receptor recognition
AUTHOR(S): Gembitsky, Dmitry S.; Lovas, Sandor; Ahmed, Shawn; Ryder, Caroline; Kopin, Alan; Murphy, Richard F.
CORPORATE SOURCE: Department of Biomedical Sciences, Creighton University School of Medicine, Omaha, NE, 68178-0405, USA
SOURCE: Peptides 2000, Proceedings of the European Peptide Symposium, 26th, Montpellier, France, Sept. 10-15, 2000 (2001), Meeting Date 2000, 109-110. Editor(s): Martinez, Jean; Fehrentz, Jean-Alain. Editions EDK: Paris, Fr.
CODEN: 69EDWK; ISBN: 2-84254-048-4
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The β-turn and C-terminal functionalities of gastrin peptides required by the human CCK2-receptor were evaluated. The stabilization in gastrin was readily accommodated by the human CCK2-receptor. The Phe residue at position 17 is essential for binding to the human CCK2-receptor. The Gly18 at the C-terminal end of the gastrin precursor was tolerated by the human CCK2-receptor. A free carboxyl group on the Gly18 was preferred by the human CCK2-receptor to an amide.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 13 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1994:69923 CAPLUS
DOCUMENT NUMBER: 120:69923
TITLE: Partial agonism by gastrin for a cholecystokinin receptor mediating pepsinogen secretion
AUTHOR(S): Tang, Laura H.; Miller, Melissa D.; Goldenring, James R.; Modlin, Irvin M.; Hersey, Stephen J.
CORPORATE SOURCE: Sch. Med., Emory Univ., Atlanta, GA, 30322, USA
SOURCE: American Journal of Physiology (1993), 265(5, Pt. 1), G685-G872
CODEN: AJPHAP; ISSN: 0002-9513
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Isolated gastric glands from rabbit were used to characterize the functional cholecystokinin (CCK)-like peptide receptors that mediate pepsinogen secretion. Pepsinogen secretion was stimulated by both CCK octapeptide sulfate (CCK-8) and A-71378, a selective CCK-A-type receptor agonist, with similar mean EDs (1.0 and 0.8 nM, resp.). Compared with CCK-8, gastrin-17 (G-17-I) showed reduced potency and only partial efficacy for stimulation of pepsinogen secretion while inhibiting the maximal CCK-8-stimulated response. The nonpeptide inhibitors, asperlicin and L-364,718, inhibited pepsinogen secretion with identical pA2 values for antagonism of both CCK and gastrin, indicating that both peptides interact with the same functional receptor. Specific binding of [3H]CCK-8 to isolated chief cell membranes was displaced fully by both CCK and gastrin, indicating full receptor occupancy by both peptides. A novel synthetic peptide analog, pseudogastrin [(Glu)5-Ala-Tyr-Nle-Gly-Trp-Nle-Asp-he-NH2], was used to investigate the structural basis for the lower potency and efficacy of G-17-I. The potency of CCK and gastrin analogs for pepsinogen secretion was dependent on both sulfation of a tyrosine residue and the position of the tyrosine residue relative to the COOH-terminal phenylalanine amide. The efficacy appears to be determined partially by the extended NH2-terminal sequence of G-17-I. The results of the present study are interpreted to show that pepsinogen secretion is mediated by a CCK-A-type receptor and gastrin acts at the same receptor as a partial agonist.

L2 ANSWER 17 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1988:161840 CAPLUS
DOCUMENT NUMBER: 108:161840
ORIGINAL REFERENCE NO.: 108:26447a,26450a
TITLE: Binding of gastrin17 to human gastric carcinoma cell lines
AUTHOR(S): Weinstock, Janet; Baldwin, Graham S.
CORPORATE SOURCE: Ludwig Inst. Cancer Res., Melbourne, 3050, Australia
SOURCE: Cancer Research (1988), 48(4), 932-7
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Gastrin-17 was bound by 5 cell lines derived from human gastric carcinomas, and the affinities of these lines for gastrin range 0.2-1.3 μM. Cholecystokinin octapeptide bound to the cell line Okajima with an affinity similar to gastrin-17, whereas shorter gastrin analogs bound with reduced affinity. Binding of gastrin was unaffected by acetylcholine, histamine, or a number of other hormones with the exception of insulin which inhibits binding with an 50% inhibitory concentrate of 0.5 μM. The ability to bind gastrin with affinities in the micromolar range appears to be a property widespread among other tumor cell lines.

L2 ANSWER 18 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1987:568938 CAPLUS
DOCUMENT NUMBER: 107:168938
ORIGINAL REFERENCE NO.: 107:26962h,26963a
TITLE: Structure-activity studies of C- and N-terminal fragments of cholecystokinin 26-33 in guinea pig isolated tissues
AUTHOR(S): Gaudreau, P.; St-Pierre, S.; Pert, C. B.; Quirion, R.
CORPORATE SOURCE: Res. Cent., Notre-Dame Hosp., Montreal, QC, H2L 4K8, Can.
SOURCE: Neuropeptides (Edinburgh, United Kingdom) (1987), 10(1), 9-18
CODEN: NRPPDD; ISSN: 0143-4179
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In vitro structure-activity studies with cholecystokinin (CCK)/gastrin-related peptides, including C- and N-terminal fragments of CCK 26-33, were undertaken in guinea pig gallbladder and ileum. The general order of potency in both smooth muscle prepns. is CCK 26-33 > CCK 1-33 > CCK 27-33 » nonsulfated CCK 26-33 > pentagastrin > CCK 30-33. None of the CCK fragments exhibit antagonistic properties such as in guinea pig, rat, and mouse pancreatic acinar cells and hog duodenum. These observations suggest the existence of CCK receptor sub-types in peripheral tissues.

L2 ANSWER 21 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1969:427672 CAPLUS
DOCUMENT NUMBER: 71:27672
ORIGINAL REFERENCE NO.: 71:5097a,5100a
TITLE: Feline gastrin. An example of peptide sequence analysis by mass spectrometry
AUTHOR(S): Agarwal, Kanhiya L.; Kenner, George W.; Sheppard, Robert C.
CORPORATE SOURCE: Univ. Liverpool, Liverpool, UK
SOURCE: Journal of the American Chemical Society (1969), 91(11), 3096-7
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Gastrin (17 nanomoles) from cat antra was analyzed for amino acid content. The amino acid sequence was then determined unambiguously on a submicro sample (100 nanomoles) by mass spectrometry: Glu-Gly-Pro-Trp-Leu(Ala,Glu4)Ala - Tyr(SO3H)-Gly - Trp-Met-Asp-Phe - NH2. A rapid (1-hr.) technique of N-methylation is described which employs the addition of MeI immediately after combining a solution of Me2NAc (to which NaH has been added) to a solution of the acetvlated peptide also in Me2NAc.

L2 ANSWER 22 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1969:430682 CAPLUS
DOCUMENT NUMBER: 71:30682
ORIGINAL REFERENCE NO.: 71:5677a,5680a
TITLE: Structure and synthesis of canine gastrin
AUTHOR(S): Agarwal, Kanhiya; Kenner, George W.; Sheppard, Robert C.
CORPORATE SOURCE: Univ. Liverpool, Liverpool, UK
SOURCE: Experientia (1969), 25(4), 346-8
CODEN: EXPEAM; ISSN: 0014-4754
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The 5-heptadecapeptide amides were synthesized for comparison of their enzymic fingerprints with those of the natural hormone to determine the structure of canine gastrin, which is derived from porcine gastrin by

substitution of alanine for glutamic acid. The compds. were prepared by the method of Anderson et al. (1966). The 5-octapeptide derivs. were prepared by active ester condensations and coupled, after saponification of the Me ester, with the C-terminal tetrapeptide. The protective groups were removed with CF3CO2H and the N-terminal pentapeptide was added by means of PyGlu-Gly-Pro-Trp-Met-N3 (PyGlu = pyroglutamyl). The compds. were purified by chromatog. on G-25 Sephadex, and 0.1 mg. samples were digested with papain at pH 7, subtilisin at pH 8, and thermolysin at pH 8 and examined by electrophoresis on Whatman number 1 paper. Comparison with digests of canine gastrin showed that [Ala8]-isomer was most similar in behavior. The fully protected 5-17 tridecapeptide amine was prepared by standard methods, and unblocked and neutralized with Bu3N. The penta-(tributylammonium) salt was coupled with the hydroxysuccinimide ester of butyloxycarbonyl tryptophan in anhydrous HCONMe2 and the remaining 3 residues were added in a single unit. All 7 fragments from both the natural and synthetic gastrins were analyzed for amino acid composition and the structures were assigned by end-group determination, or by comparison with synthetic materials. This degradation provided complete independent evidence of the correctness of the [Met5, Ala8]-sequence. No differences were detected between the synthetic heptadecapeptide amide and natural, or desulfated, canine gastrin. The structures of both canine gastrins are fully defined as PyGlu-Gly-Pro-Trp-Met-Glu2-Ala-Glu2-Ala-Tyr(R)-Gly-Trp-Met-Asp-Phe-NH2 (I, R = H), and I (R = SO3H), resp.

L2 ANSWER 24 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1966:86016 CAPLUS
DOCUMENT NUMBER: 64:86016
ORIGINAL REFERENCE NO.: 64:16228f-h,16229a
TITLE: Human gastrin: isolation, structure, and synthesis. Synthesis of human gastrin I
AUTHOR(S): Beacham, J.; Bentley, P. H.; Gregory, R. A.; Kenner, G. W.; MacLeod, J. K.; Sheppard, R. C.
CORPORATE SOURCE: Univ. Liverpool, UK
SOURCE: Nature (London, United Kingdom) (1966), 209(5023), 585-6
CODEN: NATUAS; ISSN: 0028-0836
DOCUMENT TYPE: Journal
LANGUAGE: English
AB cf. preceding abstract Synthetic human gastrin I (I) was prepared and compared to natural I. Z-tryptophan (Z = benzyloxycarbonyl) condensed with leucine Me ester by means of dicyclohexylcarbodiimide gave Z-Trp-Leu-OMe (II) which was reduced to remove Z and elongated to Pyroglu-Gly-Pro-Trp-Leu-OMe (III) by a procedure analogous to that used in the synthesis of porcine gastrin (Anderson, et al., CA 62, 6555b). (Glu-OR)4-Ala-Tyr-Gly-OMe (IV) (R = tert-Bu) treated with α-2,4,5-trichlorophenyl-γ-tert-butyl-tert-butoxycarbonylglutamate gave tert-butoxycarbonyl-Glu-Or.IV (V). Selective saponification of the Me ester group of V gave the acid (VI). The mixed anhydride of VI with diphenylphosphoric acid was coupled with Trp-Met-Asp-PheNH2. The product was treated with 98% HF 1 h. at 20° to give (Glu)5-Ala-Tyr-Gly-Trp-Met-Asp-Phe-NH2 (VII) (purified by successive chromatog. on Sephadex G-25 in 0.4% NH4HCO3 and aminoethylcellulose, elution with 0.4-2.0% NH4HCO3). III treated with hydrazine and diazotized gave the pentapeptide azide (VIII). VII-Et3N was coupled in HCONMe2 at 0° with 2 equivs. VIII. After 18 h. a second equal portion of VIII was added and the mixture left at 0° 3 days. The product (IX), purified by chromatog. on aminocellulose, was indistinguishable from natural I by electrophoresis. A lower homolog containing 4 glutamic acid residues was clearly different. IX had the same physiol. activity as I and both gave the same degradative products on

treatment with papain.

L2 ANSWER 25 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1965:498845 CAPLUS
DOCUMENT NUMBER: 63:98845
ORIGINAL REFERENCE NO.: 63:18257f-g
TITLE: Gastrin: Structure and synthesis
AUTHOR(S): Demling, L.
CORPORATE SOURCE: Med. Klin., Krankenhaus Bad Cannstatt, Stuttgart, Germany
SOURCE: Deutsche Medizinische Wochenschrift (1965), 90(40), 1783-4
CODEN: DMWOAX; ISSN: 0012-0472
DOCUMENT TYPE: Journal
LANGUAGE: German
GI For diagram(s), see printed CA Issue.
AB In a review, it was pointed out that the whole spectrum of the physiol. activity of gastrin depends on the tetrapeptide sequence: tryptophanmethionine-asparagine-phenylalanine carboxamide, appearing at the so-called carboxyl end of the mol., and the properties of the compound (gastrin I differs from gastrin II only by the absence of an esterification with H_2SO_4 at the tyrosine group) were altered if the amide group was lacking. 8 references.

L2 ANSWER 26 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1966:77255 CAPLUS
DOCUMENT NUMBER: 64:77255
ORIGINAL REFERENCE NO.: 64:14523f-h
TITLE: Synthesis of peptides related to gastrin
AUTHOR(S): Anderson, J. C.; Barton, Moira A.; Hardy, P. M.; Kenner, G. W.; MacLeod, J. K.; Preston, J.; Sheppard, R. C.
CORPORATE SOURCE: Univ. Liverpool, UK
SOURCE: Acta Chimica Academiae Scientiarum Hungaricae (1965), 44(1-4), 187-95
CODEN: ACASA2; ISSN: 0001-5407
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Isolation from hog antral mucosa of 2 closely related polypeptides, hormones gastrin I and gastrin II, both of which are many times more active than histamine in stimulating gastric secretions in conscious dogs and human subjects, has led to structural and synthesis studies. Structural studies on gastrin II are consistent only with the following amino acid sequence for the hormone, Glu-Gly-Pro-Try-Met-Glu-Glu-Glu-Glu-Glu-Ala-Tyr-Gly-Tyr-Met-Asp-Phe-NH_2. Noteworthy features of the tentative structure are the complete absence of basic amino acid residues (even the terminal group is masked), and the relatively high concentration of acidic amino acids. The structure of gastrin I was also studied and had a similar amino acid sequence except that it contained a tyrosine mol. in place of the tyrosine-O-sulphate found in gastrin II. The 2 substances are not identical, are easily separable by chromatography, and have slightly different electrophoretic mobilities.

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STN INTERNATIONAL SESSION SUSPENDED AT 09:58:27 ON 04 APR 2008